CANCER.

ITS VARIETIES,

THEIR HISTOLOGY & DIAGNOSIS

HENRY ARNOTT, F.R.C.S

THE

HISTOLOGY AND DIAGNOSIS

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BY

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ILLUSTRATED BY

LITHOGRAPHIC AND WOOD ENGRAVINGS FROM DRAWINGS BY THE AUTHOR FROM NATURE.

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1872.

PREFACE.

The substance of the following pages was originally contributed in a series of papers to the 'Medical Times and Gazette,' and my object in writing them was to endeavour to fill what seemed at the time to be a gap in English medical literature upon a subject of the highest interest.

In remodelling these papers to make them more suitable for their present form, I have thought it well to make some additions. Thus, I have inserted an account of the tumour Myxoma, because I have found that it is still commonly confounded with so-called Colloid Cancer; and I have given a brief account of the simplest mode of examining morbid growths microscopically, being persuaded that many surgeons avoid such investigations from an erroneous idea of the time and labour required for them.

I have also appended to the accounts of minute structure a practical Summary of the more important relations existing between the histology and the clinical history of new growths.

My unusual opportunities as Surgical Pathologist and Registrar during some years at the Middlesex Hospital, at a time when attention was being specially directed to the subject, are a sufficient apology for my venturing to bring forward opinions of my own upon matters requiring so much practical observation.

The confusion which has resulted from the new nomenclature of tumours will not subside until we are more generally conversant than is the case at present with the distinctions which the great extension of microscopic research has ren-

dered necessary. To succeed, in however small a degree, in clearing up that confusion would be a sufficient reward to me for any pains which have been bestowed upon this work, but a far higher object has been in my mind throughout.

Hitherto our modes of treatment of Cancer have been confessedly unsatisfactory; and so long as our ignorance of the pathology of the disease prevented us from being able to suggest a reliable prognosis in most cases, the results of the various remedies from time to time proposed could not possibly be fairly weighed; for when a remedy appeared to be successful, there always remained a doubt as to the nature of the tumour treated, and, consequently, of the share of the remedy in its removal.

Of course it is not suggested that our difficulties in this regard are as yet in any great degree overcome. Much patient experimental research is before us, ere the truth of the recent views of the local nature of Cancer, as opposed to the notion of a specific blood disease like syphilis, can be either established or refuted. But we have assuredly made great advances in the right direction; and it is not too much to hope that, as accuracy in diagnosis advances, rational and successful treatment may follow in its wake.

I am glad to take this opportunity of thanking the Council of the Pathological Society of London for permission to insert in the present work many of the drawings which I originally prepared in illustration of observations recorded in the 'Pathological Transactions.'

HENRY ARNOTT.

May 30th, 1872.

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DESCRIPTION OF THE PLATES.

With one exception (Plate IV, fig. 2) all the drawings in these plates are from microscopical sections magnified 220 diameters, *i.e.* viewed with a Powell and Lealand's $\frac{1}{4}$-inch objective and low eye-piece.

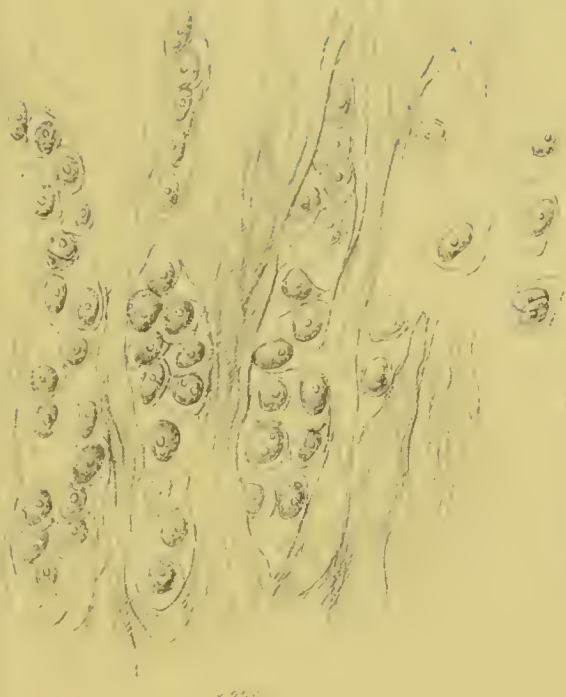
PLATE I.

Fig. 1.—A thin section from a scirrhous carcinoma of bone. The drawing shows the fibroid stroma with elongated meshes, the cells of an epithelial type, and the absence of visible intercellular material, which are characteristic of carcinoma. At one point the stroma has given way, and some of the cells have escaped. The irregular shape of the cells, with the uniform large oval nuclei and bright nucleoli, are well seen in this section.

Fig. 2.—Another section from the same tumour, showing the same fibroid stroma (*d*) and cells (*c*), but in addition a spicule of bone (*a*), probably of new formation, containing lacunal cells (*b*) with rudimentary canaliculi.

Fig. 3.—From an ossifying sarcoma of the spindle-cell type. In this portion of the tumour the spindle cells have given place to a smaller round- and oval-cell structure (*b*), from which the lacunal cells of the new bone (*a*) are apparently derived.

Fig. 4.—A thin section from the edge of the same spindle-cell (*b*) sarcoma, showing the considerable admixture of cells of other shapes (*c*) not unfrequently met with, and also showing how the muscular fibres (*a*, *a*) in the vicinity of the new growth are invaded by it. The genuine infiltration of normal tissues is here as well marked as it is in any carcinoma. The arrangement of the cells, however, the amount of visible substance separating them, and the absence of any fibroid stroma, sufficiently distinguish this growth from carcinoma as shown in fig. 1.



x 220

x 220

4

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PLATE II.

FIG. 1.—Section taken from the margin of a spindle-cell sarcoma. The upper part of the drawing represents the structure of the bulk of the new growth, whilst the small cells (*a*) stretching out into the adipose tissue (*c*) show one mode of infiltration and growth of sarcoma, namely, by "indifferent granulation material" invading the neighbouring tissues.

FIG. 2.—A strip of newly formed cartilage from near the margin of the same spindle-cell growth. This drawing, with fig. 1 of this Plate, and figs. 3 and 4 of Plate I, show how different are the structures occasionally met with in the same tumour (see p. 12).

FIG. 3.—Thin edge of a section of a remarkable spindle-cell sarcoma, the great feature of interest in this tumour being the number of huge irregular cells intermingled with the spindle-cells. At *a* and *b* two of these larger cells are seen detached, rendering their wide departure from the ordinary type the more noticeable.


1
3
2
× 220
b

PLATE III.

Fig. 1.—Section from a soft complex tumour of the parotid. A few well-formed cartilage-cells are seen imbedded in the midst of gelatinous tissue, imperfectly resembling fœtal mucous tissue. This tumour, like the growth represented in the foregoing plates, is an example of the admixture of different varieties of connective tissue often present in the same morbid growth.

Fig. 2.—Section from a gelatinous, semifluid portion of the same tumour, showing an open web of large-branched myxomatous cells, often called colloid.

Fig. 3.—Section of a spindle-cell sarcoma, in which the transition is seen from the ordinary fusiform cells of connective tissue to the larger, plumper, more densely aggregated cells of the new growth.

Fig. 4.—A bit of a pure myxoma pressed beneath the thin covering glass, and showing the entangled meshwork of very delicate fibres and branched cells which formed the bulk of the tumour, viscid glairy fluid, having the chemical characteristics of mucus, filling the interstices. It will be seen that the difference between this structure and that represented in woodcuts 10 and 11 of colloid carcinoma is very striking, although the aspect of the two growths to the unaided eye may be very similar.

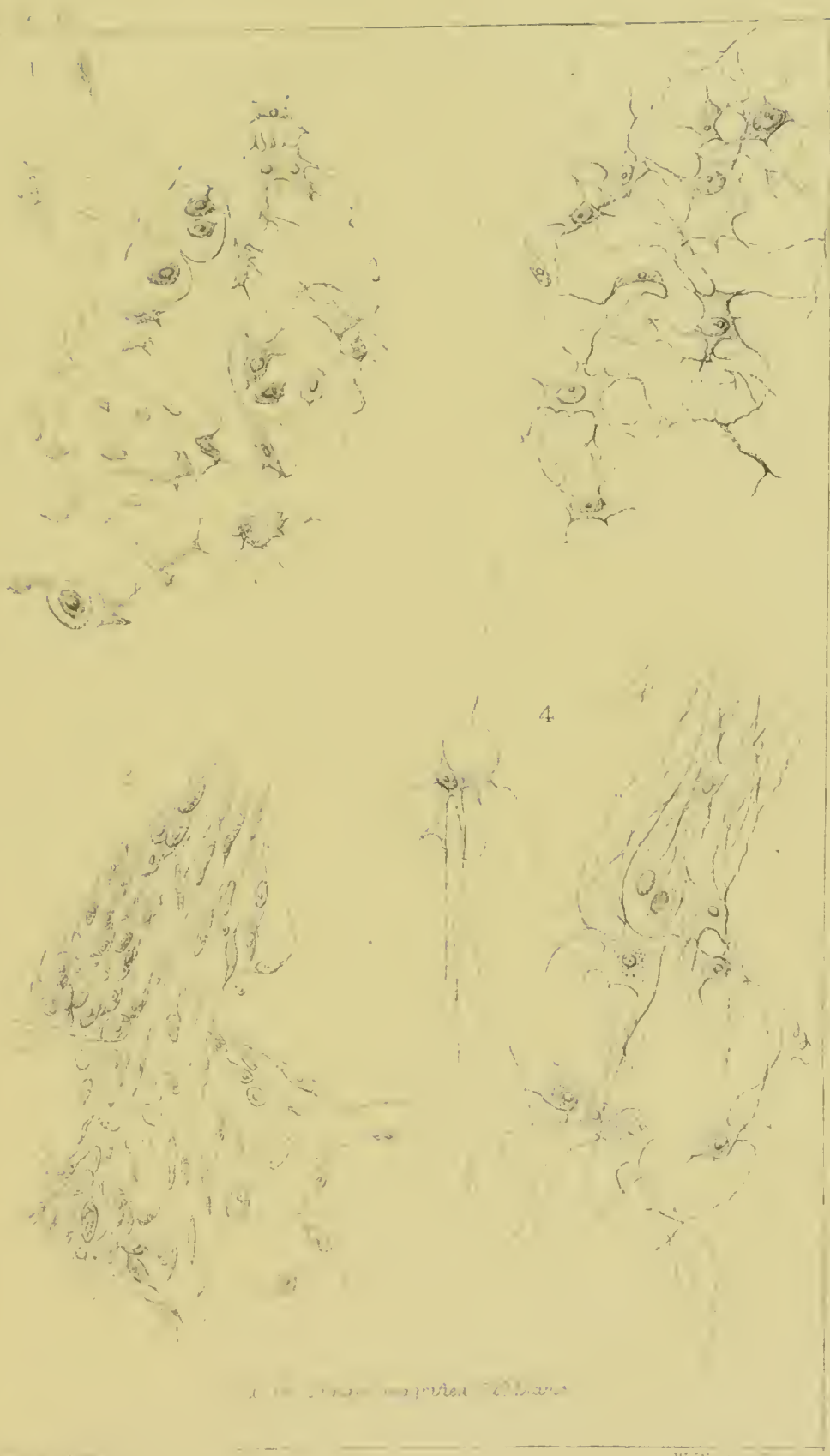

PLATE IV.

Fig. 1.—Thin section of the indurated tissue resulting from chronic inflammation or irritation of connective tissue.

Fig. 2.—Portion of the same magnified 400 diameters.

These sketches are introduced here because they show a structure very commonly met with in the investigation of new growths. Indurated and enlarged lymphatic glands, the seat of long-continued irritation from a neighbouring cancer, but without participating in the special disease, present this appearance. It will be seen in fig. 1 that as the fibroid stroma increases the corpuscles become more scarce, until ultimately the tissue assumes the form shown in fig. 2, very few corpuscles being enclosed in the small meshes of a dense, almost homogeneous fibroid material, in which no nuclei are discernible.

The same drawings indicate the average appearances presented by lymphomatous growths.

Plate IV.

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PLATE V.

FIG. 1.—From an epithelioma of the intestine. In this drawing, taken from the submucous portion, the stroma is furnished by the proliferated connective tissue of the part, whilst the contained cells, some of which exhibit a double nucleus (*a*), are probably derived from the elements of the tubular glands, and are bathed in the retained turbid fluid glandular secretion.

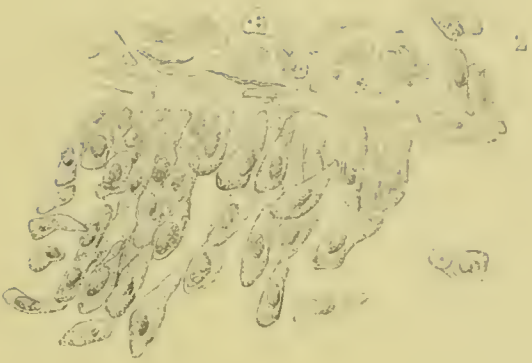
FIG. 2.—Shows the active epithelial proliferation on the surface of the mucous membrane in the same case. In the rapid overgrowth which is taking place the normal regular columnar cells are losing somewhat their characteristic shape, whilst their volume is greatly augmented.

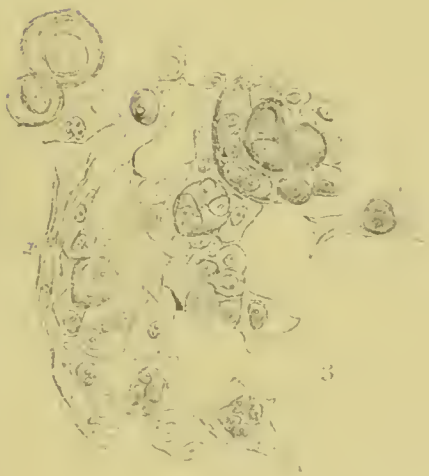
FIG. 3.—A thin section from an epithelioma of the lung secondary to disease of the clitoris. The large squamous cells, many with multiplying nuclei, and with a tendency to the formation of "nests," are precisely similar to the elements met with in the primary growth in this case, and in the inguinal glands which soon took part in the disease. A fragment of elastic fibre from the lung tissue is seen at *a*. In other of the lung nodules the "nest" bodies were well developed.

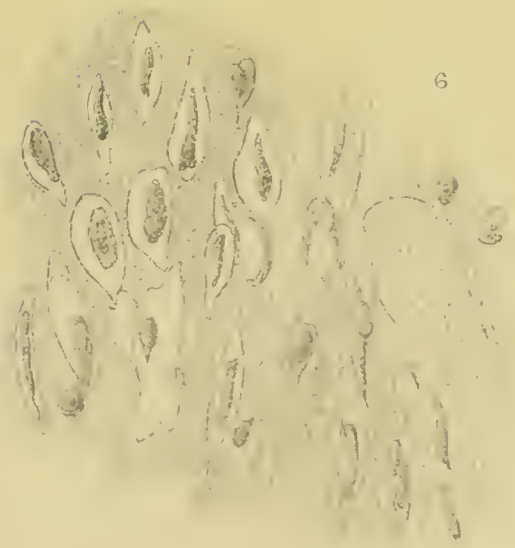
FIG. 4.—A thin section of a very soft carcinoma of the breast after hardening and staining. The cells, in their size, shape, and arrangement, cannot be distinguished from those of a scirrhus of the breast; but the fibroid stroma, which in the latter case occupies so prominent a position, is here barely distinguishable, slender homogeneous fibrils interlacing to form wide and deep loculi, in which the cells are packed.

FIGS. 5 and 6.—Sections from the malignant enchondroma referred to in page 11, occurring primarily in the testis, and subsequently affecting the lymphatic glands and lungs. Fig. 5 shows the large-celled cartilage structure of part of the growth, whilst fig. 6 shows the transition to the spindle-cell tissue which formed the bulk of most of the smaller secondary tumours in the lungs.

Plate V.







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CHAPTER I.

Introductory—Necessity for an Anatomical rather than a Clinical Classification of Tumours—The Degrees of Malignancy met with—Local Recurrence—Lymphatic Gland infection—General dispersion; various modes in which this may be brought about.

The title of this work suggests at once the difficulties to be encountered by the writer and the corresponding allowances to be made by the reader; for it is the fact that at the present time no term is used more vaguely and yet with more caution and misgiving, both by pathologists and by practical surgeons, than the term "cancer." Here in England the old clinical significance is still fondly adhered to; and although on the Continent a far greater number of surgeons recognise a definite anatomical structure to be implied by the term cancer, yet few venture to settle by any distinct form of words what that structure is, and a considerable number protest altogether against the attempt. The common argument of the practical surgeon is something like this:—"When I speak of a cancer, I mean a tumour which will return if I cut it out, which will probably also appear eventually in certain internal organs, and against which I am well-nigh helpless in any effort to eradicate it from the system. As for anatomical characters, it is enough for me

that the tumour infiltrates the tissues amongst which it grows. The precise form of its microscopic cells and the relations of these to each other and to surrounding parts are to me points of no moment." The reply of the pathologist—that chemistry having failed us, no truly scientific classification of tumours can be made upon other than an anatomical basis, and that nothing short of a careful microscopical discrimination will suffice for this—finds small favour with the surgical utilitarian; for he knows full well the difficulties which have beset those engaged in the endeavour to arrange this anatomical classification, and he fails to see what practical good will result when the work shall have been successfully accomplished.

Now I think that in this matter we surgeons might very profitably take a lesson from the physicians. It is only quite lately, long since the microscope has come into general use in medicine, that the various diseases of the lung formerly grouped under the heading "Consumption," or "Phthisis Pulmonalis," have been recognised and classified; and, although the old term may still be a convenient one for common use outside the profession, I suppose that few physicians will long rest satisfied with being told that a given case is one of phthisis. They will further ask whether it be a catarrhal pneumonia, or an interstitial pneumonia, or a chronic tuberculosis, and the answer to the inquiry will greatly affect the prognosis as well as the immediate treatment of the case. Just in like manner it behoves us to recognise that we can no longer content ourselves with the assertion that a given case is one of "cancer." As a vague term implying a malignant tumour, it may be clinically serviceable to retain it in common parlance; but we must not forget that there are as many forms of cancer, in the clinical sense of the word, as there are of phthisis; and to give a reliable prognosis—nay, even to decide upon the suitable treatment—we must look further: we must see to what special class of malignant growths the case properly belongs. It is the main object of this book to present, in as clear a

way as possible, the present stage of this inquiry; and, in order to render it practically useful, I shall avoid as far as possible entering into the disputes of the schools and all the more recondite problems which suggest themselves to the pathologist, and limit myself to a brief account of the structure and mode of growth of the common forms of malignant tumours, and the manner in which this structure may most readily be made out, briefly hinting at the same time at the bearing of the subject upon the diagnosis and prognosis of the several varieties.

In order to clear the ground for an anatomical classification, it may be pointed out at once that what may be termed the *clinical* classification is extremely defective. What, for instance, can be more unsatisfactory than a diagnosis which must await for its confirmation the return of the tumour or the infection of distant parts of the body? And if we are told that the confused blending of the tumour with the surrounding structures, causing adhesion to the skin and parts adjacent to the growth, are sufficient evidences of malignancy, I reply that even this sign is very delusive; for I have seen a growth so harmless to health as the "recurrent fibroid" of Sir James Paget, infiltrating the fat and muscle in its neighbourhood as completely as the most virulent cancer; and, on the other hand, I have seen an apparently encapsuled cartilaginous growth in a testicle followed by numerous secondary growths in the lumbar glands and lungs. Moreover—and this is the point to which I wish to draw special attention, and I would that we could speak more dogmatically upon it—amongst the infiltrating tumours, some are far more truly malignant than others, and the degree of this malignancy, in other words the prognosis of a tumour, can, in many instances, only be definitely settled by the microscope. Of course, it is not meant by this that the microscope is an infallible guide in the prognosis of tumours; if it were so, no surgeon could honestly practise his art without its aid. Within the last few years, instances of malignancy associated with almost every kind of new growth—excepting, perhaps,

the simple lipoma or tumour of adipose tissue[1]—have been recorded to the confusion of surgeons; but these instances must be regarded as exceptions to ordinary pathological rules, and need not in any way deter us from trying, at some no distant period, to deduce from the large number of rapidly accumulating observations certain general laws as to the relation of anatomical structure to clinical history and symptoms.

In our investigation of these tumours the term malignancy will be in constant use. Let us, then, pause on the threshold of our inquiry to settle definitely what especial meaning we attach to the word. By "malignancy," then, we imply such an energy of growth as baffles in a greater or less degree the surgeon's interference. And it is convenient to speak of three degrees of malignancy—viz. (1) The persistent recurrence *in loco* after apparently complete removal by the knife; (2) the tendency to infection of the nearest chain of lymphatic glands with the same morbid growth; and (3) the possible combination of one or both of these conditions with a proneness to the formation of other like tumours in distant parts of the body, and especially in the lungs and liver. Each of these degrees of malignancy may be profitably considered at the outset, in order that subsequent reference to them may be rendered more intelligible.

Firstly, the persistent recurrence *in loco* after careful removal by the knife. It has been sought to place the "recurrent" tumours in a class by themselves, as including a series of growths less malignant than cancers, but yet mysteriously prone to local recurrence after ablation.

Certainly, I have myself ceased to be surprised at the frequent recurrence of many tumours since the attention

[1] And even here we must speak with caution; for Mr. Curling has narrated a case in which a fatty tumour recurred five times in the scrotum, in spite of very careful removal. This case was reported upon for the Pathological Society of London by Mr. Campbell de Morgan and Mr. Hulke; and, in the opinion of these pathologists, the recurrence was to be explained by an active connective tissue growth accompanying the fat development, this active growth spreading from a pedicle which in each instance had been cut through.

of the profession was strongly directed to the influence of inadequate operations on the theory of cancer by the late Mr. C. H. Moore. In his paper bearing this title, in the 'Transactions of the Medical and Chirurgical Society,' Mr. Moore pointed out how constantly the local recurrence of cancer after amputation of the breast was demonstrably due to the disease germs left behind by the operator; and if he had been spared to us a few months longer, he would have seen a very remarkable corroboration of his views in the facts furnished by the novel process of skin-grafting for the healing of ulcers. Indeed, when we witness the wonderful effect of a few epidermis scales scraped from the skin and applied to the granulating surface of an ulcer (as has recently been done by Mr. Henry Lee, at St. George's Hospital)—a nucleus of new skin being formed by these few apparently dried cells—it seems wonderful that a scirrhous carcinoma should ever be satisfactorily removed by operation, its cells having so very slight cohesion, compared with that of the elements of most other new growths.

Perhaps the clearest light is thrown upon the habit of these tumours by the practice of examining thin sections of hardened tissues rather than scrapings from freshly-cut surfaces.

I have so often, on making thin sections through the margin of a growth and into the adjacent structures, discovered a real infiltration of microscopic elements where no naked-eye confusion of tissues had been apparent, that I am satisfied that the great majority, if not all, of the instances of speedy recurrence *in loco* familiar to surgeons is, not that the tissues of the part have taken on a special tendency to the production of a morbid growth which is not to be arrested by free use of the knife, but that, in fact, elements of the growth are left behind by the operator, and sooner or later develope into fresh tumours. Let me give two illustrations of this kind of infiltration. I had not long ago an opportunity of examining some secondary tumours in the lungs of a patient dying with what was said to be cancer of the uterus. The peculiarity about the secondary growths was

that each was apparently encapsuled, shelling out readily on squeezing the lung, and presented none of the ordinary characters of blending with the surrounding lung tissue met with in most cancers. Careful examination, however, showed that the growths were wholly made up of small spindle cells, and that cells exactly similar to those of the tumours were to be traced shooting out freely amongst the connective tissue of the alveolar walls and vessels of the neighbouring lung tissue. On another occasion I remember assisting at an operation for the removal of a soft tumour recurrent amongst the muscles of a woman's buttock. The growth appeared to be clearly encapsuled; at least, there was no great difficulty in enucleating it from its bed and turning aside the muscles stretched about it. Nevertheless, this was already a recurrent affair, and since that time three more operations have been performed upon the same woman. This led me to make a careful examination of the tissues surrounding the growth, and partly removed with it at one of the later operations. I found the structure of the tumour to consist entirely of the oat-shaped cells constituting the growth known to English surgeons by the name "recurrent fibroid;" and stretching out into the fat and muscle on all sides were crowds of similar cells, invading and breaking up the muscular fibres and separating the large oil-cells of the adipose tissue; in fact, the tumour was a genuine infiltrating growth.[1] Here, then, was at once the explanation of the proneness to return which had been so repeatedly manifested, for the infiltration had probably been present in the earlier tumour, although possibly in a less degree. And the examination of these and similar cases surely teaches us this great practical lesson—namely, that, excepting perhaps in distinctly encysted growths, the surgeon can hardly err on the side of too free use of the knife in the removal of tumours; nay, one may even affirm that the old operators who removed with one sweep of a red-hot knife the whole of a cancerous breast, with its covering skin, more truly served their patients

[1] 'Path. Trans.,' vol. xxii, p. 271.

than do such modern surgeons as are careful to remove only the scirrhous nodule, leaving the nipple and as much skin as possible, that the gaping wound may not unnecessarily alarm and disfigure the patient.

Of course, in thus attempting to explain the frequent cause of immediate recurrence of tumours (what Thiersch has called "continuous recurrence") by particles of the morbid growth being left behind by the operator, it is not intended to deny that cases may, and undoubtedly do, arise from time to time in which, after an absolutely complete removal a similar growth may spring up in or near the cicatrix after a lapse of many years, from the same causes which led to the formation of the primary growth ("regional recurrence"). Such subjects, bearing as they do on the ætiology of new formations generally, may well be avoided in the present essay which professes to be purely practical, and I only refer to the point lest it should be thought that such a mode of recurrence is absolutely denied.

The second degree of malignancy, in which the nearest chain of lymphatic glands is infected with the morbid growth, offers also some points for consideration; and, in the first place, it is to be noted that the disease occurring in the glands is invariably of the same nature as that of the primary tumour from which the infection has spread. At least, in all the cases which I have myself examined this has been the case, and I have not met with a single reported exception to the rule which has borne the test of careful scrutiny. It is, indeed, very seldom possible to trace the morbid elements extending along the lymphatic vessels. I have seen two cases in which the lymphatics were visibly distended with what seemed to be cancerous material; once leading from a scirrhous breast to the axillary glands, and another time stretching away from a soft cancer of the uterus; but such easily recognisable examples of lymphatic infection are very rare.

When it is stated that the disease affecting the lymphatic glands is always identical with that forming the primary

tumour, it must be borne in mind that this does not exclude instances of medullary or soft carcinoma appearing in the axilla secondary to a scirrhous nodule in the breast. The real identity of hard and soft carcinoma (restricting the term to its anatomical sense) will hereafter be considered; but it may be mentioned at once that the secondary growths spreading from a scirrhous cancer are hardly ever so hard as the original tumour, and they may present very various degrees of softness without losing their distinct anatomical structure.

Again, certain cases occasionally present themselves in which the lymphatic glands, swollen and indurated, yet gradually subside after the removal of the tumour which apparently infected them, and these are sometimes said to be instances of cancer of the glands, disappearing upon the removal of the primary cancer. From what we know of the nature and habit of cancer, however, it is not probable that this ever takes place. It is more likely that these are glands in a state of what Dr. Sanderson has called fibroid induration, due to prolonged irritation—a condition frequently met with apart from any malignant disease, and due to a certain pathological process, in which the delicate fibrillar network which normally supports the corpuscular elements of the gland becomes enormously thickened and increased, gradually pressing aside the corpuscles, and materially affecting the function of the gland (Plate IV).

The diagnosis of such enlarged and indurated glands, from glands the seat of carcinomatous growth, may be often very difficult. The main points to be relied upon are the absence of tenderness, and the fixation to surrounding parts, especially to the skin, causing the dimpling and brawny hardness usually present in the more advanced stages of carcinomatous infiltration.

Comparatively harmless though this state of induration may appear, there are not wanting those who regard it with considerable suspicion. Thus, Mr. Birkett has known a case of return of cancer in the glands five or six years after the

removal of a scirrhous breast, the glands at the time of the operation showing no signs of genuine cancerous infection. And MM. Cornil and Ranvier attach still greater importance to this fibroid induration, as lending support to their view of the connective tissue rather than the epithelial origin of cancer. Perhaps the point of greatest practical importance in this connection is the comparative frequency of lymphatic gland implication in the several forms of malignant disease. This is a question requiring much further investigation and more numerous observations than are as yet at our disposal. Dr. Billroth, the eminent pathologist of Vienna, was one of the first to draw attention to the fact that sarcoma in its spread very seldom infects the lymphatic glands, or at least not until late in the course of the disease. I have examined a considerable number of cases of malignant growths with special reference to this point, and my observations, so far, accord entirely with this view. I have once seen well-marked secondary enchondroma in the lymphatic glands, and I have rarely seen cases of true anatomical carcinoma confirmed by microscopic evidence in which the neighbouring lymphatic glands were not at length obviously infected. But amongst the sarcomata I have only thrice seen anything like distinct lymphatic gland implication, which was confirmed by microscopic examination. Two of these specimens were instances of sarcoma growing in the uterus, and presenting the usual characters of uterine cancer; and the third was a case of melanosis, in which, together with multiple tumours occurring in the subcutaneous connective tissue all over the body, the lymphatic glands generally were secondarily affected with the disease; and it is worthy of remark that in anatomical structure this morbid growth was just on the border-land between true cancer and round- or oval-celled sarcoma, very little visible matter separating the cells of the soft and juicy tumours.

This tendency to infect the lymphatic glands, which is sufficiently strongly pronounced in epithelioma, but extremely constant in carcinoma, has been amply accounted for in the

latter case by the researches of MM. Cornil and Ranvier. These pathologists, by means of specially prepared thin sections of scirrhus stained with nitrate of silver, have clearly demonstrated that into the minute alveoli which, packed with cells, form the characteristic structure of this form of cancer, lymphatic vessels open, offering a direct and easy means of conveying the special juices, and possibly cells, of the cancer to the nearest lymphatic glands. From these remarks it will be gathered that the question of lymphatic gland infection is of more than mere pathological interest. It becomes of genuine value in discriminating between carcinoma and the various forms of growth simulating that disease.

On the third or highest degree of malignancy, in which there seems to be a general infection of the system, growths springing up in various parts of the body, there is not much to be said that is not commonly received without question—for its bearing upon the doctrine of the local or constitutional nature of cancer need not be discussed here.[1] The theory of a constitutional disease with local manifestations is a pure hypothesis, and need not detain the practical surgeon for its discussion, since such a view should not for one moment deter him from adopting such means as are at his disposal for the removal of such local manifestations. Granted, for the sake of argument, that a certain taint of the system—a "blood disease," or what not—is the cause of the appearance of the tumours, still it is the tumour which kills. Mention is, indeed, not unfrequently made of death from cancerous cachexia; but who ever saw such a death? Surely the only obvious causes of death in cancer are the pain, the exhausting and fœtid discharges, the mental anxiety,

[1] For a more complete review of the evidence to be adduced in favour of the local nature of cancer (as opposed to the view of a general contamination of the blood, breaking out in many different places), and the important bearing of this doctrine upon the principles of treatment of malignant tumours, the reader is referred to a paper by the author in the 'St. Thomas's Hospital Reports,' vol. ii, 1872, "On the Therapeutical Importance of Recent Views of the Nature and Structure of Cancer."

the enforced deprivation of fresh air and exercise, and all such unavoidable results of the presence of a rapidly growing malignant tumour. And it has been well and forcibly said by one who is himself a believer in the predisposing cancerous cachexia, that he who would hesitate about removing a cancerous tumour because of the constitutional taint underlying it, would show about as much wisdom as the man who, discovering an escape of gas through the wall of a given pipe in his house, should refuse to stop it because, with gas circulating all over the dwelling, fresh escapes might be expected at any moment, either at the patched place or elsewhere!

It should be mentioned that the secondary growths are always essentially of the same nature as the primary. I lay some stress upon this fact, because it has been stated by writers of repute that this is not an invariable rule—that, for example, the secondary growths of epithelioma or epidermis cancer assume the form of encephaloid carcinoma. This is, I believe (excepting, perhaps, in extremely rare instances, which are capable of another explanation), erroneous. The secondary formations in epithelioma will always be found to present more or less closely the characters of the primary disease, when subjected to microscopic examination, and I have myself seen in the muscular tissue of the heart as perfect "nests" of squamous epithelium as are to be met with in the most typical "sweep's cancer" of the scrotum. In making this statement, however, I am reminded of a case in which a primary cartilaginous growth in the testicle was followed by secondary spindle-cell growths in the lungs (see Plate V, figs. 5 and 6). This sounds at first like a contradiction of what has been already stated, but I believe that it may be readily explained in the following way:

It has been said that there is no pathological product which has not its prototype in some normal tissue of the body, either in adult life or in the embryonic condition. Hence there is suggested a convenient classification of tumours or neoplasms, on the basis of the corresponding classification of the normal histological tissues. Now, the

physiological groups are three, of which the first includes all the connective tissues, the second muscle and nerve, and the third the epithelia, surface and glandular. It is with the first of these groups that we have mainly to do in the investigation of tumours, and great light is thrown upon the varieties and admixtures of certain growths by a due consideration of the normal development of the tissues from which they spring. Thus, if we remember that the group of connective tissues includes not only fibrous, areolar, and elastic tissues, but also mucous tissue, fat, cartilage, and bone, we shall be prepared to find any given peccant portion of connective tissue which is developing into a tumour producing at different times or in different spots of such new growth, rudimentary fragments of any or all of these structures, which, springing from a common stock, are yet so widely separated in their physical characters. In this way I am in the habit of explaining in the lecture-room, the curious mixture of cartilage, mucous, and fibrous tissues so often met with in the soft enchondromata of the parotid gland (see Plate III, figs. 1 and 2); and, in like manner, much of the apparent confusion in certain ossifying sarcomata becomes easily intelligible. And applying this reasoning to such cases as that under consideration, in which a primary cartilaginous tumour gave rise to secondary growths of spindle-cell tissue (in many of which, by the way, nodules of true cartilage were developed), we see that the same disposition to morbid development might perfectly well produce a cartilage mass in one place, whose cells, by transplantation, might, without any departure from recognised laws of development, grow into a spindle-cell, a fatty, or an osseous tumour in another part (see Plate V, figs. 5 and 6). It is obvious that a change in the *type* of the secondary growth would need a different explanation; but it is doubtful if such a change of type ever occurs.

These secondary growths are brought about by far most frequently by the entry of the elements of the primary tumours into the blood-stream; but this is not the only mode in which the dispersion may be effected. The four

following instances aptly illustrate some of the various conditions which may be present in different cases.

Sir James Paget[1] has narrated a case of primary cancer of the liver, in which all the growths were stained bright yellow by bile, and in which he found "numerous small cancerous masses of the same colour infiltrated in the lungs; and the small branches of the pulmonary arteries leading to these were filled with bright yellow substance, as if they had been minutely injected with chromate of lead. The accidental colour of the cancer materials in this case made their transference from the liver to the lungs very evident."

Dr. Dickenson[2] has recorded a remarkable case, in which a cystic tumour of the lumbar glands bursting some little time before death, scattered bits of the growth through the abdomen, and after death numerous tiny growths of the same nature were found adhering to the peritoneal surface of the intestines and other viscera.

Dr. Moxon[3] published, a few years since, the following instructive case. A man, aged 48, died with epithelioma of the trachea and obscure pulmonary symptoms. After death, a large friable ulcerated growth of epithelioma was found in the trachea, and scattered through the lungs at the extremities of the smallest air-tubes (a very unusual position for secondary cancer of the lung) were minute masses of precisely the same structure, clearly caused by multiplication of loose cells inhaled from the trachea growth.

Mr. de Morgan[4] has furnished us with a yet more striking case than any of these. A man had a tumour of the eye, for which the globe was removed. After removal some traces of tumour elements were found in the cut surface of the optic nerve. The man lived another year, and then died paralysed. The autopsy discovered a growth about the remains of the optic nerve, and another large growth of similar nature

[1] 'Lectures on Surgical Pathology,' 1863, p. 804.

[2] 'Path. Trans.,' vol. xxii, p. 292.

[3] Ibid., vol. xx, p. 28.

[4] Ibid., vol. xviii, p. 222.

massed about the "cauda equina" at the bottom of the spinal canal. It was evident that this last tumour occupied its very unusual position by the detachment of some cell or cells from the eye tumour (probably at the time of the operation), and their gradual drifting down in the arachnoid fluid, until entangled in the brush of nerves, they struck root, and developed the tumour which eventually paralysed and killed the patient.

Such are some of the many various ways in which the occurrence of secondary tumours may be explained, without the necessity for assuming a pre-existing general blood taint.

CHAPTER II.

Importance of Examination of Thin Sections—Simplest method by which such sections may be prepared, stained, and mounted—Value of Scrapings for diagnostic purposes, illustrated by Sketches of Elements of Scirrhous Carcinoma, Spindle Cell Sarcoma, and Epithelioma.

Before proceeding to the discussion in detail of the several varieties of malignant growths, it may be well to dwell briefly upon the importance of examining tumours by means of thin sections of hardened specimens rather than by scrapings from the fresh surface. For this purpose the surgeon must consent to take a little more trouble than is generally bestowed upon such examinations; but if the chromic acid, carmine solution, glycerine, &c., be kept in some convenient place, with one or two small glass shades to keep out dust, the whole process of cutting sections, staining, and mounting need occupy only a few minutes, and involves very little trouble or difficulty—certainly no trouble which is not amply repaid by the more accurate knowledge of structure so gained. The most useful magnifying power for general employment is the $\frac{1}{4}$-inch objective with a low eye-glass, magnifying together about 220 diameters. The sketches illustrating this book were cut from drawings made on the blocks, of tumour sections so magnified. But an inch or two-inch objective is also very convenient for giving a general view of the structure, and with a double nose-piece or lens-holder carrying both objectives, these powers may be changed at pleasure without any loss of time.

It would be foreign to my purpose were I to attempt to introduce here any account of the various processes by which tissues may be prepared for the careful examination of

their minute structure; but it may be convenient to mention the simplest way in which the practical surgeon may satisfy himself of the structure of a tumour about which he is in doubt.

The necessary apparatus comprises only (1) a strong solution of chromic acid (say 20 per cent.), (2) a little pure glycerine, (3) a case containing needles for teasing and lifting small bits, fine scissors, and a razor for making thin sections (a Valentin's knife is more convenient for tissues which are not artificially hardened), (4) a few bottles of test fluids—as ether for dissolving away fat, mineral acid for clearing off calcareous particles, acetic acid for rendering nuclei more distinct, &c., (5) a bottle of Beale's carmine staining fluid (which may be readily prepared at home, or by any chemist),[1] and (6) as many glass slides, thin covering slips, and watch glasses as may be desired.

Bits of the tumour the size of filberts are put to soak in water, to which a pale straw tint has been given by the addition of a little of the chromic acid solution; and if this be changed daily, two or three days will usually suffice to harden the softest tissue. When this is accomplished, very thin slices are taken from one or more of the bits, the razor being moistened with water or spirit, and these are either mounted at once, or set aside to soak for a few hours in a watch glass containing some drops of staining fluid. With a hooked needle the section is fished up from this fluid, rinsed in pure water, lightly poised over a bit of blotting paper to

[1] According to Dr. Beale's method half a drachm of strong liquor ammoniæ is added to ten grains of carmine in a test tube, and gently agitated over a spirit lamp until the solution has boiled for a few seconds. After the fluid has cooled, two ounces of pure glycerine, two ounces of distilled water, and half an ounce of alcohol are added and the mixture filtered. The clear deep red fluid resulting will keep for many months. But the special point desired, namely, the staining of the nuclei alone, is not always easy to secure, this property appearing to depend upon the exact proportion of alkalinity present. This staining process, however, even when not very perfectly accomplished, renders the structure of most tumours so much more distinct than it is otherwise apt to appear, that it becomes of considerable value to those who have not much leisure to devote to microscopic work.

absorb superfluous water, and laid flat in a drop of glycerine on the slide. It is then carefully covered with the thin glass and is ready for examination. If it is wished to preserve the specimen, the glycerine which may have oozed out from under the covering glass must be carefully wiped off with a damp handkerchief or bit of wet blotting paper, and Canada balsam, gold size, Bell's cement, or any other ordinary cement lightly varnished round the edges of the cover.

In thus advocating the working with sections, however, I am anxious not to underrate (as it is just now somewhat the fashion to do) the value of scrapings where more elaborate examination cannot be had. There is unquestionably much information to be gained from such stray elements as are to be scraped up from the freshly-cut surface; and when one has to give a diagnosis at once, a very shrewd guess can be made by comparing the naked-eye characters of the tumour and its mode of growth with the appearances presented by its juice. In fact, the moment a tumour is cut into, a scraping of its cut surface should always be examined with a $\frac{1}{4}$-inch glass, for this will often make further examination unnecessary for purposes of diagnosis, and in doubtful cases may render incalculable service to the operator by informing him of the nature of the neoplasm, and of the expediency of removing perhaps more of the tissues around than might otherwise seem necessary.

In illustration of my meaning I have shown in Fig. 1 a tolerably typical scraping from a scirrhous tumour of the breast. Given such a scraping from a tumour having the ordinary characters of hard cancer, and yielding an abundant milky juice on pressure, and I think the diagnosis might be almost made with safety. The chief points about such a scraping are—the diversity of the cell forms, with the tendency to an epithelial type, and the large proportion of elements in a state of fatty metamorphosis. The scraping should be made near the margin of the tumour. If from the centre, little but fatty *débris* will be seen; and if from the extreme edge,

smaller more uniform cell forms, and consequently less characteristic, will be obtained.

Fig. 1.

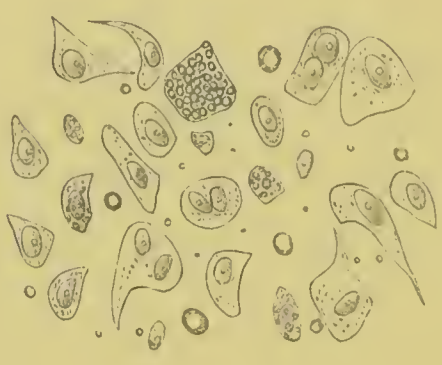

Fig. 1.—From a scraping of a freshly-cut scirrhus of the breast. Magnified 220 times.

In like manner, such a scraping as is shown in Fig. 2 will also throw much light upon the tumour yielding it. Here

Fig. 2.

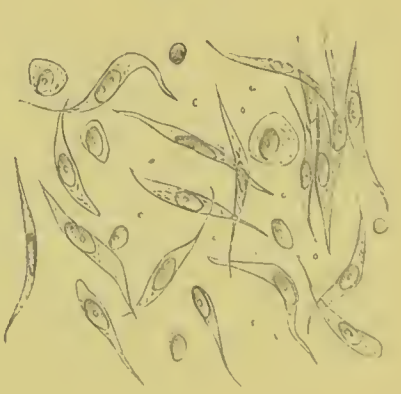

Fig. 2.—Cell-forms obtained by scraping a spindle-cell sarcoma. Magnified 220 times.

the juice is less abundant, and one is at once struck with the comparative uniformity of shape of the cells—not that in the

scraping of a spindle-cell sarcoma one gets neeessarily only spindle-cells. There are usually some few round and oval forms present, but the one type largely preponderates, and—unless the central parts of the tumour have been selected—there is much less evidence of oily change than in the former case.

And, thirdly, I suppose that there could be very little uncertainty about pronouncing a growth yielding a scanty ground-rice-like juice, with the characters shown in Fig. 3, to

FIG. 3.

FIG. 3.—Scraping from an epithelioma of the arm. Magnified 220 times.

be an epithelioma of the squamous variety. Here the large flattened cells—some of them cohering by their margins, some clustering tightly in a manner suggesting a fragmentary "nest," and many others seen edgeways, looking like hard broken fibres—are sufficient to stamp the nature of the growth without the necessity of making sections. So, also, the juice of a lymphoma, showing only small round and oval corpuscles with shreds of delicate fibres, with no large cell forms, would amply suggest a temporary diagnosis pending a more elaborate examination.

CHAPTER III.

CARCINOMA—The diagnostic value of "Cancer Cells"—Definition of Carcinoma—Its minute structure—Stroma—Cells. The stages of development, and decay.

BEGINNING with the most virulent of malignant growths, that variety of cancer familiar to surgeons under the form of scirrhus of the breast is the first to claim our attention. This is the tumour about which the hottest disputes have been waged by pathologists as to its intimate structure, etiology, and mode of growth, and by surgeons as to its curability by operation or otherwise. And this controversy has itself sufficiently demonstrated the necessity for the harmonious co-working of these two classes of observers; for it has been a common resource of those surgeons who maintain the constitutional nature of the disease and the impossibility of its cure, to assert that an alleged cured cancer has been only a chronic mammary or some other simple form of tumour; and the uncertainties hitherto attending the diagnosis of mammary cancer, even with the advantage of a microscopic examination, have rendered this process of begging the question less assailable than it is hoped it may become in future.

Since the great debate in the French Academy on the diagnostic characters of the cancer-cell, there has always been a hazy notion afloat in this country that, in spite of the conflicting views expressed on that occasion, there is unquestionably some mark distinguishing the cells of a cancer from those of any other tumour; and many of those who have given up the ancient idea of a "typical caudate form," still believe that there are certain signs—as a large eccentric nucleus, or the presence of a certain proportion of "mother" cells containing

one or more smaller ones—by which these cells may be distinguished. At the present time, however, the question troubling the pathologist is the source of these cells rather than their peculiar characters, since it is now believed that their distinctive features are to be sought in their arrangement rather than in the form of the cells themselves. Are they developed from epithelium, connective-tissue-corpuscles, or wandering white blood-cells? This inquiry has taken the place of the former, since more extended observation has shown that cells microscopically indistinguishable from those of scirrhus may be found in granulations, in certain sarcomata, in glandular growths, and even in healthy parts, as the pelvis of the kidney and the prostate. Nay, so completely has the "cancer-cell" fallen from its former position, that certain modern pathologists affirm that this form of cancer should be called "alveolar fibroma," as best expressing the real nature of its structure.

The microscopic cell of a scirrhous cancer seems to be in its younger stage a spherical mass of protoplasm containing a comparatively large oval nucleus with bright nucleolus, much resembling the cells of the *rete mucosum*, or lower layers of the cuticle; but, like these, as development proceeds, the spherical cells, closely squeezed together and increasing in volume, undergo various modifications of size and shape, according to their rapidity of multiplication and the extent and direction of peripheral pressure. The cell of scirrhus is in all respects identical with that of medullary cancer; and since these two forms of tumour, with their modifications, constitute the most important group of malignant growths, to all of which English surgeons are in the habit of applying the term cancer, it becomes necessary to use a distinct name for these most cancerous of cancers. The introduction of new names into a sufficiently complex nomenclature is, however, so great an evil, that it is perhaps wise to accept, for want of a better term, the Greek word *carcinoma*, already widely so employed, as expressing this form of cancer as defined by the microscopist, and to leave the Latin

synonym as a more vague and general term representing merely a malignant tumour. In this sense, then, the word "carcinoma" will be employed in the following pages; and this brings us to define strictly what structure it is that is so designated.

A carcinoma may be described as *a tumour in which a more or less dense fibroid growth forms a sponge-like or cavernous framework, whose alveoli are filled with loose cells of an epithelial type, grouped together disorderly, bathed in a clear fluid, and having no visible intercellular material*[1] (see Plate I, fig. 1). If it were desired to give a rough illustration of what is here meant, one might imagine a bit of coarse sponge or honeycomb filled with clear syrup, and the cells of the comb packed with soft and yielding masses, with uniform hard centres, such as would be formed by encrusting hempseeds with jelly. If the honeycomb thus prepared were slightly warmed, and then roughly pulled or squeezed, so as to render its spaces less symmetrical and the little bodies irregularly compressed, there would result a very fair representation of a carcinomatous tumour; and on cooling and cutting thin sections of such a model, the network of wax, enclosing in its meshes variously formed bodies with tolerably uniform oval centres, and a quantity of pellucid, viscid fluid, would strongly remind one of what is seen on examining thin sections of carcinoma under the microscope. Bearing this illustration in mind, it is easy to understand the abundant milky juice which exudes from a freshly-cut scirrhus, as also the large number of cells which float out into the surrounding glycerine when a thin slice of fresh carcinoma is mounted for examination; and the scanty cohesion between these cells

[1] This definition differs from that of MM. Cornil and Ranvier, in describing the cells as being of an epithelial type, in laying stress upon their disorderly arrangement, and in insisting upon the absence of visible intercellular substance. These modifications are not opposed to the views of Virchow, Lücke, or Rindfleisch; and I venture to think that they are of service in excluding lymphoma, adenoma, and alveolar sarcoma—growths which, from their possessing alveolar stroma enclosing cell-elements, might be included by any less strictly worded definition.

further explains their fatal tendency to transplantation to distant organs, being easily hurried away in the lymph- or blood-stream which may reach them.

There are thus offered for examination two main structures in carcinoma—the fibroid framework or stroma, and the cells which it encloses.

About the nature of the fibroid *stroma*, whether it consists merely of the compressed connective tissue basis of the diseased organ, or whether it is a genuine new growth, various opinions have been held. It seems a matter of comparatively small moment. My own observations certainly incline me to regard the stroma as without doubt for the most part a portion of the new growth. Numerous specimens in which the stroma has coloured far more deeply with carmine than the cells, others in which (as in fig. 5) it has been formed of delicate spindle cells, and others, again, in which attempts to trace the development of the several elements have seemed to show me the growth of this stroma proceeding *pari passu* with that of the contained cells, have left little doubt in my mind on this point. This stroma differs a good deal in density and in structure in different specimens; and it is in the proportion of the fibrous to the cellular elements that the distinction between hard and soft carcinoma exists.

In its most typical form, as obtained by pencilling out a

FIG. 4.

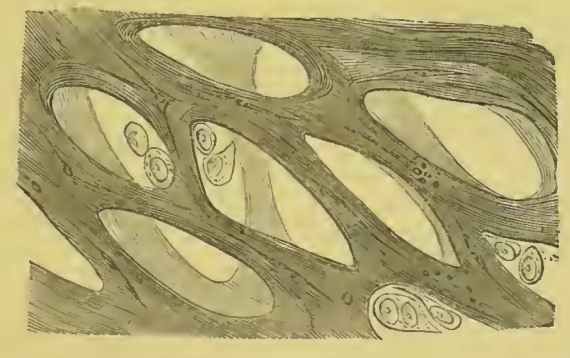

FIG. 4.—The alveolar fibrous stroma of carcinoma, obtained by pencilling out, under water, a very thin section of a scirrhous tumour of the breast. Magnified 220 times.

thin section of scirrhous breast under water, the stroma is seen to have a delicate fibrillated appearance (fig. 4), in which are a few spindle-shaped corpuscles, specially observable at the junction of the alveoli. The thicker parts of such a section show similar bands half out of focus, and a comparison of many such sections seems to show that this fibroid substance forms a cavernous system throughout the tumour. In other cases the fibrillation is less apparent, and we have then a homogeneous texture, like that forming the tough substance of a chronic inflammatory product, as in the lung of so-called "fibroid phthisis" (Plate V, fig. 4; Plate IV, figs. 1 and 2). More rarely this meshwork is made up of beautiful elongated spindle cells (see fig. 5). I have twice

FIG. 5.

FIG. 5.—Rare form of soft carcinoma, in which the stroma is made up of delicate spindle cells. Magnified 220 times.

seen this structure, each time in a medullary carcinoma of the breast. As to the form of the alveoli, these may vary as greatly in shape as in size. In the majority of sections from hardened specimens, the spaces will be more or less oval or

elongated, and (probably as the result of the action of the hardening reagent) the cells will often retreat slightly from the walls of the alveoli (fig. 7), rendering the outline of these more clearly discernible. The injections of Thiersch and Billroth have shown this stroma to be abundantly supplied with vessels, and, as might be *à priori* supposed, the delicate vessels in medullary carcinoma, as in other soft new growths, lacking the support afforded by the denser fibrous tissues of the firmer varieties, are prone to aneurismal dilatations, and the frequent rupture of these weakened vessels gives rise to the many varieties of colour and consistence which characterise such tumours. The observations of MM. Cornil and Ranvier as to the relation of the minute lymphatics to the alveoli, and the important bearing of this point upon the question of extension of the disease, have been already mentioned. The stroma is also often the seat of an abundant infiltration of the same small spherical cells, which by their grouping give rise to the first appearance of carcinoma.

The cells of carcinoma are more remarkable for their multiformity of contour and size than for any special peculiarity distinguishing the individual cells. The eagerness with which students look for "mother cells," or multiple nuclei, as the cells *par excellence* of cancer, soon gives place to the expectation of seeing very few of these—and, indeed, they are comparatively seldom met with save in the most rapidly-growing softer forms. Perhaps the most constant shape is a slightly compressed oval, five or six times as large as a white blood-corpuscle, with a single large oval nucleus, and a bright nucleolus; but in the later stages the cell becomes larger and, in consequence, more irregular in outline (fig. 6). In the earlier stages of the disease it is common to find the cells small, and of a tolerably uniform oval shape, but arranged in the same way in the meshes of a fibrous stroma. A special attribute of all these cells is a proneness to speedy decay. Hence it is difficult to make a scraping from a divided scirrhous breast which shall not contain many

cells more granular than they should be, and some few whose nuclei are obscured by the little bright oily particles which

Fig. 6.

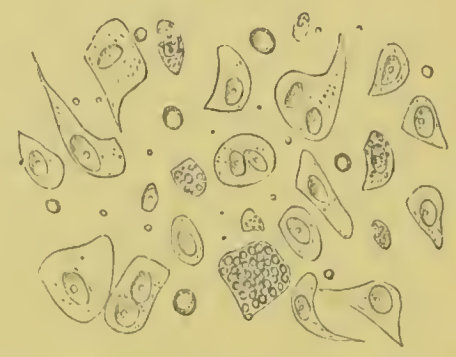

Fig. 6.—Various cell-forms from a carcinomatous tumour. Magnified 220 times.

in others so fill the cells as to render its parts wholly undistinguishable.

Having thus briefly described the typical stroma and cells of ordinary carcinoma, it is perhaps hardly necessary to state that these are not found in all the perfection of their most typical arrangement in every section of a carcinomatous tumour. Reference has been already made to the fact that the main distinction between hard and soft carcinoma lies in the proportion of the fibrous to the cellular elements. In the softer growths it is sometimes difficult to make out any fibrous stroma at all without careful pencilling, so delicate are the bands and so wide the meshes (see Plate V, fig. 4). In well-marked scirrhus, on the other hand (as shown in fig. 7), the alveolar arrangement is particularly conspicuous (see also Plate I, fig. 1). But in both of these cases it often happens that, from some defect in the mode of preparation or obscurity caused by excessive staining with carmine, the precise forms of the individual cells are by no means so easy to define as they are shown in these woodcuts. What one frequently sees is merely a number of dark clusters of cells, of which perchance the nuclei may be tolerably clear, imbedded

in a pale, homogeneous, or fibrillated medium; but here much help is obtained by looking round the margin of the

Fig. 7.

Fig. 7.—Typical mature carcinoma, from a scirrhous breast. Probably by the action of the chromic acid solution employed to harden the specimen, the cells have shrunk away from the alveolar wall to some extent. Magnified 220 times.

section—for even if this be not sufficiently thin (and the edge of the roughest razor-section is generally fine enough for the purpose), the loose cells which float out abundantly into the glycerine in which the section floats are readily discernible, and display perfectly the shapes which are obscured in the denser portions of the specimen.

Again, in some parts of such a tumour, field after field of the microscope will exhibit only a flat surface of fibrous texture in varying stages of development, and then, perhaps, a few irregular groups of cells will herald the approach of a confused mass of richly cellular structure, which may again as suddenly give place to considerable tracts of connective tissue, or remains of mammary gland, if it be a scirrhus of the breast which is under observation. Moreover, if the

section be taken from the extreme margin of the scirrhous nodule some such appearance as is shown in fig. 8 is seen—

Fig. 8.

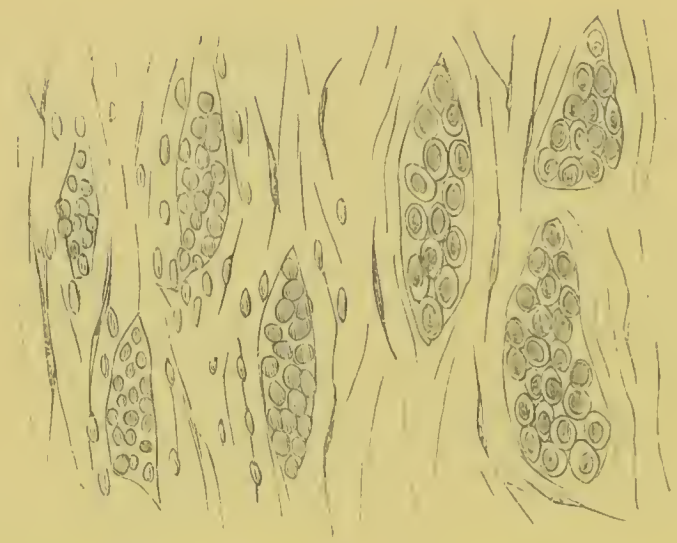

Fig. 8.—Developing carcinoma, from the extreme margin of a scirrhous nodule. The fibrous tissue to the left of the sketch is seen to be dotted with minute granular corpuscles, which are also collected in groups. To the right are the young, oval, nucleated cells of the tumour, arranged in elongated alveoli. Magnified 220 times.

namely, a distribution through the fibrous tissue of small spherical corpuscles very like leucocytes (the "indifferent granulation material" of Virchow), at first in twos and threes, but soon in larger clusters, until these seem to change into the groups of larger oval nucleated cells, which are not very different from those of mature carcinoma. I say "seem to change" advisedly, for it is very difficult to trace accurately these tissue transformations, and many eminent observers ascribe the origin of the cells of scirrhus to the glandular epithelium, whilst others are equally confident of their development from proliferating connective-tissue elements. It must be remembered, also, that recent observations upon the nature of leucocytes or wandering white blood-corpuscles render it possible that these furnish the starting-points for

the cells of carcinoma as for those of many other new growths.

It is scarcely necessary to discuss here the argument from this last hypothesis which might forcibly suggest itself to those who hold cancer to be a "blood disease." Just as we are beginning to be doubtful about the wisdom of dismissing the terms "exudation" and deposit," in favour of terms expressing more definitely the idea of local cell-proliferation, so it may be that the recent remarkable experiments of Professor Cohnheim and his followers may bring us again to accept the theory of a "blood disease" as the essential cause of the formation of malignant tumours; but it may be at least suggested that even if the first cells of a cancerous tumour be emigrants from the capillaries, the condition which determines their special development when once outside the vessel must depend solely upon some local change or aptitude or force in the tissues amongst which they are extravasated, for the same emigration of white blood-corpuscles is seen to be the first step in many widely different processes, as in inflammation and in the repair of wounds. In the present unsettled condition of pathological research, when the discovery of to-day is too apt to be classed with the mistakes of yesterday, we may be fairly excused some reluctance in accepting too unreservedly deductions from experiments made by different observers with conflicting results. Under these circumstances, it is prudent to confine ourselves to a statement of what is actually seen in an ordinary specimen of developing carcinoma, and not to trouble ourselves for the present about the true interpretation of these phenomena.

To sum up this hasty review of the microscopic structure of carcinoma, its several stages of development, maturity, and decay may be illustrated by the accompanying diagram (fig. 9).

First, we have an accumulation of small bodies resembling granulation corpuscles, which may be leucocytes or (more probably) the product of connective-tissue proliferation (*a*).

These gradually form small clusters, and the next appearance is a series of groups of larger oval and nucleated cells (*b*). These, in their turn, give place to well-marked meshes in the fibrous material, filled with irregular densely-packed cells (*c*),

FIG. 9.

FIG. 9.—Diagram representing the several stages of carcinoma. *a*. Granular corpuscles collecting into groups (connective-tissue proliferation?). *b*. Young oval nucleated cells clustered together. *c*. Typical mature structure. *d*. Gradual withering by fatty degeneration of cell elements and shrinking of alveoli.

the typical structure of carcinoma, and no sooner are these formed than symptoms of decay appear, the cells become gradually obscured by oily accumulation within them, burst, and the oil runs into larger drops; lastly, the connective-tissue corpuscles in the stroma may themselves degenerate; and then (*d*), we have merely a granular fibroid stroma enclosing spaces filled with oil particles, and in which the arrangement of the remains of the alveoli alone suggest to the observer the carcinoma which has flourished and withered.

I have said that this form of malignant disease is specially typified in ordinary scirrhus of the breast, but the appearances

of carcinoma as it affects other tissues, as bone or muscle, undergo certain modifications, and these will be now described, together with those "accidental" conditions of carcinoma to which have been assigned special names, as colloid, villous, osteoid, melanotic, &c. One need hardly enter with any detail into the consideration of the naked-eye characters and clinical features of ordinary breast cancer. To the hospital surgeon the clinical characters of scirrhus are but too well known. The careworn woman who applies with a "lump in the breast," and who displays on uncovering her wasted form the shrivelled, hard gland, with sunken nipple and puckered skin, and who then complains of "kernels in the armpit," and of failure of health and strength, is too familiar an object to need description here, and the many varieties of appearances occasionally met with are amply set forth in such classical works as that of Sir James Paget on 'Surgical Pathology.'

CHAPTER IV.

CARCINOMA (*continued*).—Microscopic Appearances modified by Tissue affected, as Muscle, Bone, &c.—Villous Cancer—Hæmatoid Cancer, or Fungus Hæmatodes—Melanotic Carcinoma—Colloid—Myxoma.

BEFORE entering upon the brief consideration of the varieties of carcinoma to which have been assigned special names, some notice should be given to the modifications caused by the locality or tissue affected by the growth. It has been already said that the secondary growths met with in the liver or lungs are, as a rule, more richly cellular than the primary tumour; but, excepting that the stroma is less obvious, there is very little other difference discernible, either in the form or size of the cells, or in their arrangement. Sometimes, when the development of these secondary tumours is exceedingly rapid, an unusual preponderance of the small cells before described may be met with. I have seen, for instance, a very rapidly growing carcinoma recurrent near the scar of an amputated breast, in which the cells were so uniform in shape and so small in size that it would have been very difficult to name the growth at all without the aid afforded by the examination of the primary tumour. In the outlying pea-like nodules which occasionally occur in the pectoral muscles beneath a scirrhous breast, and which afford such beautiful opportunities for the study of the infiltrating characters of carcinoma, it often happens that the bulk of the tiny mass is made up of these small "indifferent cells," with merely a trace of the alveolar fibrous stroma so characteristic in mature carcinoma.

Carcinoma affects bone either in the form of distinct

tumours or as an infiltration of the bone with cancer elements, so as to affect its consistence rather than the shape of the bone. In such cases of bone-softening in connexion with cancer elsewhere as I have had the opportunity of examining, I have seldom been able to detect any cancerous elements, but occasionally one meets with instances of considerable deformity of the flat and long bones occurring as either primary or secondary carcinoma.[1] In such cases there is an abundant milky juice to be scraped from the section of the softened bone, and in this juice are just such cell-forms as are commonly met with in the juice of a scirrhous tumour. Very thin sections of bone so diseased show groups of such cells enclosed in spaces corresponding to the Haversian spaces of the original bone; but, besides this, the osseous lamellæ are occasionally found to be divested of calcareous matter, and to form a fibrous stroma very like that of ordinary carcinoma, the lacunæ being swollen into groups of new cells in some parts, as though these cells resulted from the proliferation of the original lacunal cell. In other cases of primary carcinoma of bone a structure precisely resembling ordinary scirrhus is met with, the fibrous stroma being replaced more or less largely by interlacing spicules of new bone (see Plate I, fig. 2). To follow up in detail the modified appearances of carcinoma as they are altered by the tissue affected, however, would lead us beyond the scope of these sketches. With the brief suggestion that the statement of Virchow, as to the absence of any visible intercellular material being an essential condition of true carcinoma, is probably not to be received without exception, since one occasionally meets with instances of undoubted scirrhus of the breast in some parts of which a certain amount of granular material separates the cells, we may pass on to the notice of those named varieties of cancer whose distinguishing characteristics are caused by degenerative processes or other accidental conditions.

Villous Carcinoma has been described, but is, I fancy, an

[1] For a remarkable case of this kind see 'Path. Trans.,' vol. xix, p. 356.

extremely rare variety. Malignant villous tumours are almost invariably associated with epithelioma rather than with carcinoma, and are met with on such mucous surfaces as are normally villous—the villi, owing to the disturbed nutrition of the part, becoming greatly hypertrophied. Certainly many tumours which are called villous cancers are simply due to a more or less active overgrowth of the healthy villi of the part, which may give rise in the bladder or rectum to large masses of velvety substance, forming beautiful objects when floated out in water, but having no trace of malignancy about them, either in their anatomical structure or clinical history.

At the same time it must be mentioned that villous tumours of the bladder and elsewhere have been described by Prof. A. Lucke and others, in which groups of carcinoma cells were imbedded in the fibrous matrix of the papillæ; and such growths would be quite rightly named villous carcinoma.

Hæmatoid Carcinoma or *Fungus Hæmatodes* may be dismissed with a very few words. Very soft and rapidly growing tumours, whether carcinomatous or sarcomatous in type, are supplied with very delicate capillary networks, and these fine vessels, when separated by careful washing from the cell-elements of the growth, are seen to be variously dilated, the vessel wall yielding in the direction of least support. This is particularly the case where fatty degeneration advances as rapidly as the cell-proliferation, and it is specially in such instances that, the vessels bursting, large quantities of blood are poured out, and by their subsequent changes diversify with such rich colours the cut surfaces of these growths. It is obvious that this accidental hæmorrhage is an insufficient ground for according a special name to tumours exhibiting it, for precisely the same thing happens in a greater or less degree with every soft new growth.

But I will take this opportunity of directing attention to those growths occasionally met with, in which the blood so poured out plays so important a part amongst the various

characters of the tumour that the elements of the new growth are in danger of being overlooked. I have twice seen tumours of this kind, each time in the ham or lower part of the thigh, and both times with similar symptoms. A swelling had been present for some weeks or months, and latterly had rapidly increased. It presented all the signs of a cystic growth or large abscess, but on making an exploratory incision a stream of pure blood flowed forth, and the surgeon thought that he had opened an aneurism. On pressing upon the artery in the groin and enlarging the opening, a large sac of blood was discovered, with clot-layers enclosing it, and in one case the surgeon was with difficulty induced to believe in the true nature of the disease, and amputate the limb. In both cases, however, a comparatively insignificant basis of spindle-cell sarcoma was found infiltrating the muscular tissue, and it was from the new vessels of this growth that the blood had evidently been poured; and in one of these cases death occurred after three or four years from sarcomatous growths disseminated through the viscera.

Melanotic Carcinoma.—This form of disease is exceedingly rare. The great majority of cases of "black cancer" are really instances of sarcoma, and will be referred to with the other sarcomata. When a true carcinoma is melanotic, the black tint is due to a certain proportion of the cells containing granules of pigment; but almost all the dark nodules in carcinomatous growths which have come under my own observation have derived their colour from the changes resulting in blood extravasated into the part, and could not be strictly classed with melanotic growths at all.

Colloid Carcinoma.—This very interesting variety is probably much less common than is usually affirmed, for most English surgeons have unquestionably been in the habit of placing in this class those purer forms of mucous tumour or myxoma which bear to the naked eye a close resemblance to jelly, in the clear flickering masses sometimes met with. The true colloid also owes its characters

to the presence of mucus, but in the form of a degeneration; and a colloid tumour bears to a myxoma much the same relation that a fattily degenerated fibrous tumour does to a lipoma.

Thus it is that, besides such very characteristic examples of colloid cancer as have been best described by Mr. Sibley, in his admirable paper in the 'Medico-Chirurgical Transactions,' we meet with colloid nodules in many examples of carcinoma and sarcoma, and also in cases of epithelioma; and even single cells are sometimes the seat of this change, appearing amongst the polymorphous carcinoma cells, with large refracting clear spaces within them, distending the whole cell, or giving the impression of a greatly dilated nucleolus. Where this change is general, a peculiar jelly-like aspect is imparted to the growth, which can yet be seen to be a genuine infiltration. Thus, I have seen a portion of a very extensive colloid carcinoma in the abdomen (its usual seat) distinctly infiltrating the muscular tissue of the uterus, growing from the peritoneal surface, and invading the organ to a depth of some lines. The effect of this accumulation of mucus within and between the cells is to alter the microscopic appearances as greatly as the coarser characters. Single oval cells become enormously distended, the nucleus remaining near the periphery, and the rest of the swollen cell being marked with faint concentric lines (possibly indicating successive stages in the mucous accumulation), and in this way a figure resembling an oyster-shell is produced (fig. 10). When a multi-nucleated cell is affected, the group of nuclei is surrounded by the same crease-like lines, and when, from the over-distension of many cells, a distribution of the contained mucus through the stretched alveoli takes place, large spherical spaces are formed, in which the remains of cells and nuclei in the centre are surrounded by these singular concentric faint lines, so that a microscopic portion of carcinoma so affected reminds one strongly of a sheet of still water, into which a few pebbles have been tossed, throwing the calm surface into a series of circling ripples, which gradually fade

into one another, and are lost (fig. 10). The fibrous stroma, however, may remain comparatively unaffected, although much stretched, and broad tracts of waving fibres with oat-

Fig. 10.

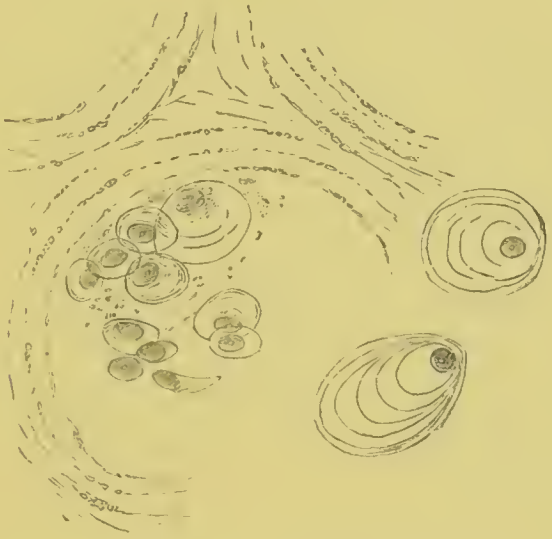

Fig. 10.—Colloid carcinoma. The two detached cells exhibit in a marked degree the change which has affected to a less extent those still grouped in an alveolus. From a colloid of the stomach. Magnified 220 times.

shaped nuclei may be traced mapping out the growth into round or oval alveoli of various dimensions (fig. 11). These appearances have gained for the tumour the name "alveolar cancer;" but it has been already shown that all carcinoma is essentially alveolar. It is only that here, the alveoli being distended with a clear fluid, their arrangement is more clearly discernible.

It is to be noted also that in some cases of colloid carcinoma the cells themselves are quite free from any but the ordinary fatty degeneration. The viscid mucoid fluid appears to be poured into the alveoli from some other source, leaving the unaltered cells squeezed into clusters in the centre of the greatly enlarged spaces. I have lately seen two beautiful

instances of this change affecting ordinary scirrhus of the breast in the practice of my colleague Mr. Croft, and in both cases one could trace the gradual increase in the size and

Fig. 11.

Fig. 11.—Colloid carcinoma, showing the fibrous stroma, whose spaces are filled with clear mucus. At one point, a few cells undergoing the colloid degeneration are shown. Magnified 220 times.

shape of the carcinomatous alveoli by the accumulation of the mucus within them until the stroma was almost entirely replaced by large tracts of the fluid in which floated the cell-clusters mentioned.

Myxoma, the growth with which these colloid degenerations are so often confounded, is a tumour of mucous tissue —the tissue which occurs so abundantly in the fœtus, but which is met with elsewhere only in the vitreous humour of the eye and in the jelly-like basis material of the umbilical cord. Similar as are the coarser characters of these tumours to those of colloid cancers, the microscopic structure is very different. Myxoma in its purest form resembles a lump of jelly limited by a very thin capsule, and separated into lobules of varying sizes by delicate curving and interlacing

fibres. When cut into, the knife drags out of the tumour long viscid strings of clear fluid, and the same fluid wells freely from the cut surface, and flows away in a bulky stream. This fluid gives the characteristic reactions of mucus; that is to say, it is coagulable by heat and vegetable acids, and forms a precipitate with mineral acids, soluble in an excess of the acid. Its mode of coagulation in spirit is also peculiar, for instead of forming dense clouds or floccuIi, as albuminous fluids do, its fall through the spirit is marked by circling streaks and slender ribands of opacity. A little bit of the fibrous stroma teased out or pressed between glasses shows a very definite structure, cells of either a spindle or irregular shape branching off into long, slender, communicating fibrils, which by their interlacing form an extremely delicate spongy tissue, pervading the tumour and holding the mucus in its meshes. Such a cell structure is shown in Plate III, fig. 4, that drawing being taken from a pure myxoma the size of a cocoa-nut, lying between the muscles of the thigh of an elderly woman. In figs. 1 and 2 in the same plate other varieties of the same tissue are represented, taken from a soft complex tumour of the parotid. Myxoma is very rarely malignant, and hence it is important to distinguish it from colloid degenerations of such formidable growths as sarcoma and carcinoma.

It happened to me, for instance, to meet with a case of pure myxoma of the breast, which had been removed for cancer, at the same time that I was engaged in the examination of the two breast specimens of colloid just mentioned, and the coarse characters of all three tumours were so very similar that it would have been quite impossible to pronounce this one to be a myxoma before a microscopical investigation revealed its structure of beautfully delicate interlacing spindle cells.

CHAPTER V.

SARCOMA.—Distinction from Carcinoma—Divided into Spindle-cell, Round- and Oval-cell, and Myeloid Sarcoma, and Glioma — Spindle-cell Sarcoma.

IN the last chapter those varieties of carcinoma which have acquired distinct names, as fungus hæmatodes, colloid cancer, and the like, were discussed, but a large number of malignant growths yet remain for consideration, which in their intimate structure are essentially distinct from carcinoma, although generally coupled with it by English surgeons under the comprehensive title cancer. The most important of these may be divided into two groups, the sarcomata and the epitheliomata; and of these sarcoma claims our first attention, as the more malignant, and, from a clinical point of view, the more nearly allied to carcinoma.

It is probable that by far the greater number of "soft cancers" and "firm medullary cancers" recorded in English publications are really sarcomas; and if we were to limit the term "cancer" to "carcinoma," as here anatomically defined, we should probably be surprised to find how very rarely true primary medullary cancer is met with by the surgeon. Nearly all melanotic growths, for instance, and all the primary soft cancers of bone, would probably be more correctly classed with the sarcomata; a fair proportion of "villous cancers," and at least a third of the cancers affecting the uterus and rectum would find a place amongst the epitheliomata, whilst all the "medullary cancers" of the eyeball in young children are really gliomas. Allusion has been already made to the clinical importance of recognising these distinctions, and it will be sufficient to repeat here

that, although all three varieties of new growth are truly and formidably malignant, they exhibit this property in very different and definite degrees.

Thus, sarcoma, although in certain of its forms nearly as prone as carcinoma to infect remote parts, very rarely invades the lymphatic glands, and probably seldom appears as a secondary tumour until a comparatively late stage in the disease; hence the greater hope of a successful issue of any operation attempted for the removal of a sarcomatous growth, provided that the affected limb be divided at a safe distance from the tumour. Where this is not possible, as in certain cases of mammary sarcoma, although the patient may live long with no visceral or glandular complications, yet the local growth itself will be very apt to return with great pertinacity; the reason being, that sarcoma is as essentially an infiltrating or tissue-invading growth as carcinoma, and equally difficult to extirpate without a freer use of the knife than is commonly deemed necessary. Mr. De Morgan[1] has suggested a rule for operative interference with these malignant tumours of the limbs. After narrating two cases of sarcoma of the lower limb before the Pathological Society of London last year, he remarked—"Are there any means of diagnosing these sarcomatous tumours from true cancerous encephaloid growths, if such exist? There can be no doubt that in the latter disease amputation should be performed through the joint, not in the continuity of the bone. I do not think it is so necessary in a case of sarcoma. At any rate, I have amputated through the bone in some of these cases without return of the disease after many years." In the same contribution it is suggested that "generally the veins are less defined, and the growth is much more rapid in a sarcoma than in an encephaloid cancer." Whether this last observation is constantly true or not, I have no means of judging, for I confess to having myself very rarely seen primary soft carcinoma of a limb; and as I have seen very many malignant growths in such positions, I am led to believe

[1] 'Path. Trans.,' vol. xxi, p. 341.

that primary soft carcinoma of the extremities is seldom met with by surgeons. In the form of secondary growths in the viscera I know of no distinguishing naked-eye character of sarcoma save the absence of umbilication. Very few carcinomatous nodules, however soft, fail to exhibit more or less dimpling of the surface from contraction of the fibroid stroma upon the cells which, in the centre of the growths, so soon fattily degenerate; but I believe that secondary sarcomatous nodules have usually no such sign distinguishing them. For the rest, these sarcomata vary in consistence from tough fibrous tissue to a creamy softness, yield to the knife scraping the cut surface an abundant milky juice, blend intimately with surrounding healthy tissues, rarely being encapsuled, although occasionally shelling out from such a tissue as the lung as though they were so limited, and in all respects bear the closest resemblance to genuine soft carcinoma.

The main distinctive characters of sarcoma, therefore, are to be sought for solely in the form and arrangement of its microscopic elements; and a sarcoma may be described as a tumour made up of embryonic tissue, which may tend towards development into a perfect tissue. Hence *a sarcoma is almost entirely a cellular growth, with more or less of visible intercellular substance,* and the cells are usually of a spindle or fusiform type.

Although the prevalence of one form of cell in each tumour is the rule, it is not uncommon to meet with considerable variety in the size and shape of the component cells in a single tumour; and in classifying the sarcomata, therefore, one must have regard rather to the *prevailing form of cell* than to the exclusive presence of any one form. Thus, one may meet with fine oat-shaped, large plump spindle, small or large oval, small round, and huge myeloid cells; and, according to the proportion in which any one of these forms preponderates, sarcomatous tumours are subdivided into—(1) *spindle-cell,* (2) *round- or oval-cell,* and (3) *myeloid* sarcomata. Besides these general varieties, sarcoma takes a

special form, and receives a special name, *Glioma*, when affecting the neuroglia or fine connective tissue of the nervous system.

In all these several varieties, however, the one character remains—viz., that the bulk of the tumour is built up of simple cells, bound together by a scanty homogeneous or granular semi-fluid substance. Hence a marked distinction from carcinoma, in which the cells are, as a rule, quite free from any visible intercellular material, and float in the meshes of a fibrous stroma. A further difference is seen in the form of the component cells. It has been already said that the cells of carcinoma are of an epithelial type. Now, cells of this kind are very rarely met with in sarcoma. One does, indeed, occasionally meet with a formidable variety of sarcoma, in which huge angular and many-tailed cells are interspersed with the spindle cells forming the bulk of the tumour; and a *scraping* of such a growth might readily mislead an observer (see Plate II, fig. 3). But, in the great majority of cases, the cells of sarcoma, when they are not simply elongated and disposed in regular tracts, are plump and round or oval rather than angular, for they are imbedded in a soft fundamental substance, and are so not subjected to the changes of form brought about by mutual pressure in the case of the cell-elements of carcinoma. The semi-solid intercellular substance also accounts for the comparatively scanty juice yielded on scraping any but the softest sarcomas. This juice is also less freely miscible with water than that of carcinoma, the cells cohering in little flakes; and, in examining thin sections, very few detached cells float out into the water or glycerine in which the section is immersed, instead of the large number of cells so detached in carcinoma.

Spindle-cell Sarcoma is by far the most common of all these tumours. Springing from connective tissue, and assuming the form met with in the development of granulation tissue into the fibrous texture of a scar, one meets with considerable differences in the size and appearance of the cells, which may vary from an extremely slender fusiform shape,

barely distended in the centre by a small elongated nucleus, to a plump cell with large oval nucleus and delicate tapering extremities. Whichever variety be present, a certain definite arrangement of the cells prevails, their axes being parallel to one another, and broad waving tracts of such parallel cells crossing and recrossing through the tumour. A scraping generally shows sufficiently the type of cell present (see fig. 12), but viewed in section the shape of the individual cells is

Fig. 12.

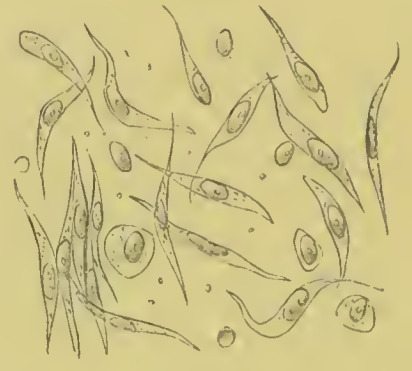

Fig. 12.—Scraping from a spindle-cell sarcoma. Magnified 220 times.

by no means always so easily made out. The regular arrangement of oval or elongated nuclei, and the occurrence here and there of patches of apparently small round cells enclosed by these others (fig. 13, *b*)—in reality similar bands running at right angles to the first, and so cut across transversely—is tolerably suggestive; but at the edges of such a section one may generally see the fine tails bristling out, if indeed there be not a free cell or two showing yet more distinctly their precise form (fig. 13). In some parts of these tumours the spindle-cell growth gradually passes into ordinary connective or white fibrous tissue, in such a manner as to render it impossible to say whether the spindle-cells are developing into the formed tissue or whether they are themselves derived from this by a retrograde metamorphosis to an embryonic condition. Besides this common admixture of connective tissue, spindle cells

usually form the basis of other sarcomatous tumours, occurring in small number, indeed, in the round- and oval-cell

Fig. 13.

Fig. 13.—Thin section of a spindle-cell sarcoma, showing in the centre groups of similar cells divided transversely. Magnified 220 times.

growths, but rarely wholly absent. A curious feature of this growth is the tendency shown by its elements to assume a larger, plumper form with each recurrence, and, together with this alteration in the size of the component cells, to exhibit an increased rapidity of growth and proneness to infiltration. So far as my own observation goes, the changes in form with recurrence are limited to these, but my friend Mr. Anderson has recorded a case in which a recurrent spindle-cell growth of the breast in its latest appearance assumed the form of the "alveolar sarcoma" of Billroth, large oval cells being contained in the small meshes of a delicate reticulated stroma.

Spindle-cell sarcoma (including, as it does, the tumours long recognised as "fibro-plastic," "recurrent fibroid," "fibro-cellular," and many of the "medullary sarcomata") exhibits very different degrees of malignancy in different

cases, so that a prognosis is specially uncertain in the case of this growth. Local recurrence may in almost all cases be predicted where the knife has not gone quite clear of the affected tissues; for this form of tumour, usually described as encapsuled, or spreading only in the connective tissue, occasionally exhibits distinct infiltration of other textures. I have myself seen instances of spindle-cell growth invading muscular tissue, and breaking up the striped fibres in quite as destructive a manner as any carcinoma (see Plate I, fig. 4). Infection of remote parts is also not very uncommon. I have met with spindle-cell growths in the liver, lungs, and mesentery; but such secondary growths are very rarely found in the lymphatic glands.

It is probable that a careful consideration of the microscopic structure offers valuable indications for a prognosis, those tumours being more apt to show true malignancy whose elements are plump and interspersed with large, irregular, and multi-nucleated cells. Special regard must, of course, be had to the rapidity of the growth, its consistence, and its seat. Where, for instance, the tumour is distinctly encapsuled, and even pedunculated—as in certain fleshy nasal polypi—the prognosis would be infinitely more favourable than where the growth infiltrates a soft, moist part, subjected to constant movement—as I have twice seen it in the uterus, simulating, in all respects, ordinary uterine cancer, and running a similarly fatal course.

CHAPTER VI.

SARCOMA (*continued*).—Round- and Oval-cell Sarcoma—Small Round-cell Sarcoma—Myeloid Sarcoma.

ROUND- AND OVAL-CELL SARCOMA—Besides the spindle-cell growth which constitutes the bulk of most of the sarcomata, certain of these tumours are made up of cells of a still lower type—embryonic cells—consisting merely of little lumps of nucleated protoplasm, which, held together by a nearly fluid connecting-material, show but little tendency to assume an elongated form by regular pressure on the sides, but remain as soft, spherical or ovoid cells, like those met with in granulations, although occasionally considerably larger; hence the name "granulation tumour," which has been suggested for this form of growth. Tumours possessing this structure are generally very soft, and from their consistence and general appearance, as well as from their microscopic characters, are more liable than any other form of neoplasm to be mistaken for medullary carcinoma. These tumours are very vascular, the vessels being usually simple channels through the cell-tissue, with walls formed by the same cells; and hence the very frequent rupture of the vessels, and escape of blood into the substance of the tumour—sometimes to such an extent as to give rise to a large "blood-cyst," which by its size may mask the real nature of its origin. The cells themselves are also very fragile, so that it is unusual to prepare either a scraping or a section of one of these growths without allowing a large number of free nuclei to escape. Seen in section, it is often even more difficult to recognise the precise

form of the cells than in the fusiform variety. The usual appearance is that of an amorphous or granular substance in which large or small round or oval nuclei, with bright nucleoli, are imbedded. At the edges of the section the rounded outline of the soft cells may be recognised, and in little detached bits of the section their shape becomes yet more distinct. The size and shape of such detached cells (see fig. 14) suggest at once the occasional difficulty in distinguishing these tumours from carcinoma.

FIG. 14.

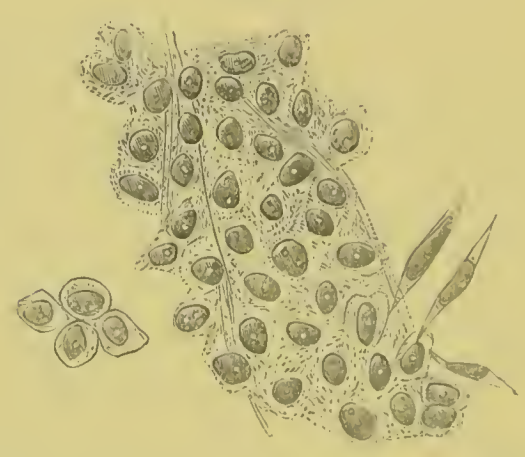

FIG. 14.—Section of large oval-cell sarcoma, with detached cells resembling those of carcinoma. Magnified 220 times.

The cells are, indeed, somewhat plumper and less like epithelial elements than are the ordinary cells of carcinoma, and there is usually some amount of visible intercellular substance; but where the stroma is fibrillated—as is sometimes the case—and fibrillated in such a way as to suggest a meshwork like the alveolar stroma of carcinoma, the distinction between the two is one of the most delicate points in pathology. Billroth has suggested the name "alveolar sarcoma" for this latter form. It is, fortunately, rarely encountered, and its accurate distinction is a matter of patho-

logical interest rather than of clinical importance, for about its grave malignancy there can be no doubt. I have seen a patient dying with upwards of a hundred of such tumours scattered through her body, chiefly in the subcutaneous cellular tissue, but also affecting lymphatic glands, breast, and kidney. In this case most of the growths contained more or less of black pigment, the pigment granules lying in large round cells, and in sufficient quantity to render the tumours distinctly melanotic.

The more usual form of round-cell sarcoma is made up of much smaller cells than those just described, cells closely resembling leucocytes or the first cells of a granulation; and since these minute cells are mostly about the size of blood- or lymph-corpuscles, the distinction between this form of growth and lymphoma (to be presently noticed) is sometimes as difficult to draw as is the distinction between the larger oval-cell sarcoma and medullary carcinoma. This small round-cell tumour differs from true lymphoma mainly in lacking the fine reticulated stroma of the latter neoplasm. The cells or corpuscles are separated by a variable amount of semi-fluid granular substance; but occasionally an appearance as of fine fibrillæ branching amongst the cells is met with, and when this is the case the growth is to be distinguished from lymphoma by the absence of minute nuclei in the angles of the network to be hereafter described as characteristic of that structure. Round-cell sarcoma is a distinctly infiltrating growth, as may be seen in the subjoined sketch (fig. 15), taken from a thin section of one of these tumours springing from the fibula and blending with the muscles of the calf. Remains of striped muscle-fibres broken up and invaded by the new growth sufficiently attest its destructive character, and show that the muscle is not merely wasted by the pressure of the increasing mass in its neighbourhood.

The structure of this tumour closely resembles what is to be met with in the vicinity of nearly all active new growths. As these advance they send before them, so to say, "feelers"

of this "indifferent granulation material," which stretch out into the surrounding structures, and form the first histological

Fig. 15.

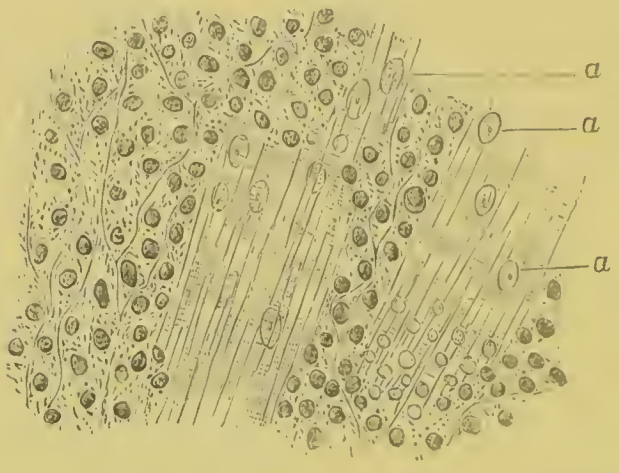

Fig. 15.—Small round-cell sarcoma infiltrating muscle; *a a a*, nuclei of the striped muscle-fibres. Magnified 220 times.

indication of the march of the morbid change (see Plate II, fig. 1). Reference has been made to this tissue in the description of the early stages of carcinoma. The peculiarity about the growth now occupying our attention is, that the whole bulk of the possibly enormous mass is made up of the same simple small corpuscular structure. To establish this fact it is of course necessary to take a scraping or section from three or four different parts of the tumour under examination. Such an investigation may show the *prevailing type of cell* to be of another kind, these small round corpuscles merely spreading about the margins of the growth; and so the tumour may receive a different name, and perchance a corresponding difference may be required in the prognosis of the case.

These round- and oval-cell sarcomas are usually very soft, white—or variously mottled by the results of blood-extravasations—blending intimately with the structures amongst which they lie, and readily exuding a creamy juice filled with

the cells and escaped nuclei of the tumour. They are far more apt to infect lymphatic glands than are the spindle-cell varieties, and, as a general rule, are also far more rapid in their destructive course.

Myeloid Sarcoma is a form of the spindle-cell variety in which a distinctive feature is given to the growth by the presence, in considerable number, of the large plate-like masses of nucleated protoplasm normal in fœtal bone-marrow. But it must be borne in mind that these singular cell-masses are met with under many different circumstances as well as in

Fig. 16.

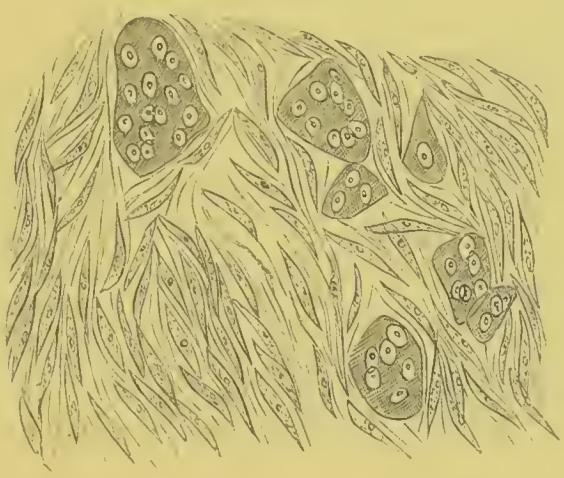

Fig. 16.—Myeloid sarcoma from an epulis. Magnified 220 times.

the tumours springing from the medullary cavities of bones. It is probable that few spindle-cell sarcomas from any part of the body could be thoroughly examined, bit by bit, without some "myeloid" cells being encountered; and Dr. Payne has described the occurrence of similar cells in certain early stages of lymphatic gland enlargement. But in certain sarcomatous tumours springing from bone, and especially from the medullary cavity of the bone, these cells occur in such number as

to offer a convenient characteristic by which to classify the growths exhibiting them.

These myeloid growths are usually much firmer than the other varieties of sarcoma, approaching more nearly to the density of fibromas; their cut surface has a smooth, fleshy look, unlike the fasciculated appearance of the firmer spindle-cell varieties, and they yield a scanty juice to the knife scraping them. They are very commonly met with springing from the periosteum of the jaw (where they are usually styled fibrous epulis) and about the ends of the long bones, but they may be met with in other situations. They are probably less malignant than many forms of sarcoma, but they are very apt to recur after apparently careful removal, and secondary growths have been occasionally met with in the lymphatic glands, lungs, &c.

Microscopically the diagnosis of this form of sarcoma is sufficiently simple. Embedded in a tissue made up of small oat-shaped cells (with which small round and oval cells may be mixed) are large pale irregular cells (fig. 16) containing small bright oval nuclei with nucleoli. These last cells have often the appearance of flat plates rather than spherical or ovoid masses of protoplasm, and vary in size from a tiny cell containing a single nucleus, to a very large mass holding a score or more of similar nuclei.

CHAPTER VII.

SARCOMA (*continued*).—Glioma; its Clinical Characters of Malignancy and Microscopical Structure—Melanotic, Osteoid, and other varieties of Sarcoma—Mixed Sarcoma.

CLOSELY allied to the small round-cell sarcoma is the special tumour of nerve, to which Virchow has given the name GLIOMA (γλία, glue), but which is still usually grouped with the medullary cancers by English surgeons. This growth proceeds from the *neuroglia*, or delicate connective tissue which supports the nervous elements of the brain and its extensions, and more frequently comes under the observation of the ophthalmic surgeon than of those of his brethren who practise general surgery. It may occur in the brain, and so give rise to the special symptoms of brain tumour, according to its position; but it is more usually encountered springing from the retina of a child—for glioma is almost wholly limited to early life, the intra-ocular tumours met with in later years being generally sarcoma, or rarely carcinoma. The child is brought to the surgeon blind, and with, perhaps, already a peculiar yellow metallic brilliancy of the pupil. Ophthalmoscopic examination reveals a whitish mass bulging into the vitreous, and interfering more or less considerably with the normal position of the lens and other parts of the eye. If now the eyeball be removed—as it should be without delay—a section through the globe will probably bring to light a pinkish-white brain-like mass, with opaque yellow spots through it, springing from some portion of the retina, projecting forwards into the vitreous, and involving to a greater or less extent the other tunics of the eye.

After hardening this structure in suitable reagents, thin

sections can be made, and it is then seen that the mass is made up of closely aggregated, very small corpuscles, round, oval, or tending in parts to a spindle form. These corpuscles are granular, with one or two bright central dots, and are embedded in a soft amorphous or obscurely fibrillated stroma. The stroma is usually so soft and scanty as to be with difficulty discerned, but about the edge of a very thin section it may happen that some of the corpuscles may be displaced, and the connecting substance is then more clearly visible

Fig. 17.

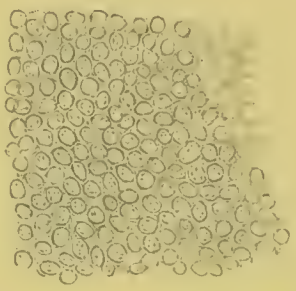

Fig. 17.—Very thin section of a glioma of the retina. Magnified 220 times.

(fig. 17). In other cases the stroma is distinctly fibrillated; and this fibrous element seems particularly developed in the secondary gliomatous growths. The corpuscles are mostly the size of leucocytes, or smaller; and, save for their delicacy and position, have little to distinguish them from the elements of round-cell sarcoma already figured. In certain cases, indeed, the cells may assume a much larger form, and, passing into spindle shapes, be wholly undistinguishable from the sarcoma elements furnished by the coarser forms of connective tissue. The yellow, opaque spots are cheesy masses, the result of the fatty degeneration of the new tissue which has, doubtless, often led older observers to call this growth "tubercle" of the eye.

From this sketch of the tumour it will be inferred that glioma should exhibit features of malignancy, just as we have seen sarcoma to do; and there are not wanting records of

cases which sufficiently justify the position of glioma amongst the cancers. Although rarely encountered as a secondary growth in the abdominal or thoracic cavities, Knapp has recorded a case of secondary glioma of the liver, and Virchow a similar growth in the kidneys, and instances of extension to the brain and of infection of the neighbouring lymphatic glands and of the bones of the face have been mentioned by other observers. Growing commonly as a single nodule in the retina, multiple growths in the same tunic have been met with, and loosened tumour-cells from a detached retina may alight upon the choroid and give rise to fresh growths in that structure. In the later stages of the disease the growth freely involves the tissues with which it comes in contact, and finally projects from the orbit as a bleeding, fungating, unsightly mass, infiltrating the parts around, and causing hideous deformity of the face.

The history of these examples of malignancy warns the surgeon not to delay an operation which may be completely successful in the eradication of the disease, if performed in time; and the practice of Mr. Hulke—to whose valuable researches on this as on other points of ocular pathology English surgeons are so greatly indebted—of dividing the optic nerve close to the foramen, and of applying chloride of zinc paste to the interior of the orbit, lest some remains of infectious material light up fresh mischief, must commend itself to all operators. This precaution is specially desirable in those not infrequent cases in which the optic nerve, divided at first close to the globe, is found swollen, with a creamy fluid oozing from its cut surface.

Occurring in the brain, glioma assumes the form of a soft roundish tumour of gray semi-translucent material, not unlike recent infiltrated tubercle, but softer, more vascular, and larger than most tubercular masses, and with less tendency to extensive cheesy metamorphosis. Microscopically the structure of the brain tumours corresponds in all respects with those developed in the retina.

Before quitting the subject of sarcoma, those varieties

which depend upon degenerative changes, or special modifications of nutrition, must be briefly noted. This is the more necessary, because such variations have usually attracted far more attention than the changes in minute structure which have been already related. The difference between a bone-like and a soft fleshy growth is much more marked than between two forms of fleshy tumour containing round or spindle cells respectively, although clinically and anatomically the latter distinction is doubtless the more important. The terms "melanosis," "osteoid cancer," and "colloid," show how much stress has been laid on these accidental conditions, and how necessary it is to study them in connection with the subject.

Melanotic Sarcoma.—It was stated, when treating of carcinoma, that by far the greater number of pigmented tumours are really sarcomas of either the round- or spindle-cell variety. In a case to which reference has been already made of a woman dying with innumerable melanotic tumours over the body, chiefly lying in the subcutaneous connective tissue, but also invading the lymphatic glands, breast, and one kidney, the cells were round or roundly oval, and those cells in which the pigment was contained were of considerable size. In this instance an old black wart was the seat of the primary manifestation, but in the melanotic sarcomata, so frequently met with springing from the choroid of the eye, the cells are more commonly of a spindle form. I once examined the head of a man dying with cerebral symptoms many months after an eye had been removed with such a growth, and I found several black masses of considerable size scattered through the brain, all of which were made up of beautifully delicate pigmented spindle-cells.

Whether the cells are round or oval, the striking fact about these growths is that the pigment granules are contained in only a very small minority of the cells, although the tumours may be as black as ink; and it is to be further noted that although the rule is that all the secondary growths are also black, the amount of pigmentation may vary con-

siderably, and some of the visceral masses may be quite pale —still, however, presenting the same cell-forms as the primary tumour. No organ is exempt from the liability to become the seat of these melanotic growths. Encountered most frequently in the subcutaneous connective tissue, the muscular tissue of the heart itself may occasionally be infiltrated with nodules of the disease, and I have seen a case in which a melanotic sarcoma of the eye was followed by the development of similar black infiltrations in nearly every organ of the body.

The great clinical indication in all examples of melanosis is to cut out the primary tumour as speedily and as widely as possible, as the early and free dispersion of the germs soon renders the extirpation of the disease impracticable.

Osteoid Sarcoma.—Bone-like sarcomata (commonly styled "osteoid cancer") may present very different structures. Springing commonly from the periosteum, or from the medullary cavity of bones, the cells may be of either of the usual forms, and the peculiar character of the growths may depend upon either a growth of true bone ramifying through the tumour as an open spongy network, or an infiltration of the intercellular material with calcareous salts.

In the latter case microscopic sections of the brittle chalky mass exhibit hardly any definite structure until a drop of dilute hydrochloric acid has been allowed to flow under the covering-glass. The observer, following the drop of acid, then perceives a copious effervescence, and, as the gas-bubbles float off the field, the confused granular network clears away, and reveals the delicate round or spindle-cells of which the tumour is constructed. No lacunæ nor canaliculi, nor other bone elements, are seen in such tumours, nor is there any cartilage or other structure suggestive of true ossification. The growth is simply an ordinary sarcomatous formation, in which the granular soft material between the cells is hardened by saturation with calcareous salts. Accordingly, although the secondary growths may be affected in the same way, it is not uncommon to meet with them

quite soft or fleshy, and exhibiting only the cell structure of the primary tumour *minus* its calcareous infiltration.

True ossifying sarcoma is more rarely met with, and presents a very different appearance under the microscope. The bulk of the growth still consisting of round or spindle-cells, with soft intercellular material, a spongy network of bone pervades the cellular structure. The new bone varies in amount in different parts of the tumour, but almost everywhere lacunæ and rudimentary canaliculi are clearly recognizable, and at the margin of the growing bony spicules is commonly either a small-celled medulla-like structure (Plate I, fig. 3), with perhaps some myeloid elements, or a cartilaginous tissue from which the bone is directly developed in the usual way. In this variety, as in the former, the rule is for the secondary formations to present a similar tendency to ossification; but here, also, the rule is frequently departed from, the remote growths often showing only the sarcomatous cell-structure of the unossified portions of the primary tumour.

It is clearly important to distinguish between the denser forms of these ossifying sarcomata and the simple osseous growths which they sometimes closely simulate; for the simple osseous tumours are probably never malignant, whilst the presence of any admixture of a soft fleshy substance having the microscopic characters of sarcoma is of grave prognostic significance, and, although by no means forbidding operation, necessitates the utmost care to insure the complete removal of the tumour. As in these cases the medullary canal of the bone is sometimes found to contain nodules of the disease at some distance from the neighbourhood of the large tumour, it would seem to be a sound rule to resect the affected bone entire, rather than to trust to sawing across it at an apparently safe distance from the morbid swelling, although, indeed, this last practice has the sanction of so high an authority as Mr. De Morgan. Even a careful resection of the entire bone will not, however, always ensure the permanent removal of the disease, for I have seen a case of osteoid tumour in the lower end of the femur following

removal of the leg for a similar tumour of the tibia. In this instance the head of the tibia, which had been unwillingly spared by the operator, was apparently free from any morbid change ten months after the first operation, when the growth in the femur had attained such dimensions as to necessitate amputation at the hip-joint.

Degenerative changes, due to fatty or mucous metamorphosis, or to the results of hæmorrhages, blocking of vessels, inflammation, or gangrene, are all commonly met with in rapidly growing sarcomas—the mucous degeneration producing a colloid appearance of parts of the tumour which is specially striking, and to which reference has been already made when speaking of "colloid carcinoma."

Mixed Sarcomatous Tumours are sometimes so puzzling to students that they need a passing reference. When one remembers that a sarcoma is merely a tumour resulting from the reversion of healthy connective tissue to a fœtal type, the cells of which continue to multiply without, as a rule, undergoing any special differentiation into a normal adult tissue, one is prepared to meet with a tendency to develope into different forms of connective tissue in various sarcomas, and even in several parts of the same tumour. Now, since the histological group of "connective tissues" includes mucous, areolar, fibrous, elastic, fatty, cartilaginous, and bony tissues, there need be nothing very surprising in meeting with a tumour presenting a combination of all these varieties more or less completely developed; and it does sometimes happen that nearly all these structures may be encountered in different parts of the same tumour. Where this is the case, the point of chief prognostic importance is the amount of primitive cell-structure showing no such development. Where this is great, the bulk of the tumour presenting a simple cellular structure, the presence of well-marked cartilage or bone here and there is no surety of the innocence of the tumour. Secondary formations, in which the spindle or other cell-forms predominate, may be expected; but where the greater portion of the tumour exhibits some one fairly

developed adult tissue (and especially where this tissue is strictly homologous—as lipoma amongst fat, or fibroma in fascia), the prognosis is more favorable, provided that the tumour itself is thoroughly extirpated.

CHAPTER VIII.

Lymphadenoma; its Clinical and Anatomical Characters—Psammoma; its Usual Seat, Structure, Innocency, and Rarity.

Lymphadenoma.—Amongst the various new formations to which surgeons have in former times given the common name "encephaloid cancer," perhaps none is still so seldom recognised as that to which the name "lymphadenoma" has been given by modern pathologists, to signify the close correspondence between the microscopic structure of this growth and that of the follicular portion of a lymphatic gland, known as the "adenoid tissue of His." It is only quite recently that special attention has been called to this variety, in England more especially by Dr. Sanderson and Dr. Murchison, and in France by MM. Cornil and Ranvier. The disease may be shortly described here as one in which soft infiltrating tumours of various sizes are scattered through the several organs and tissues of the body in a manner precisely resembling many of the soft sarcomas and carcinomas already noticed, but made up of very different and sufficiently characteristic elements.

Usually commencing in an enlargement of lymphatic glands, and often limited to such hypertrophy, many glands being matted together to form one vast mass, the morbid structure is often met with invading the internal viscera—as the spleen, lungs, liver, and kidneys—and even the muscles and bones are not always exempt from the disease. The tumours are usually of a grayish- or yellow-white colour, sometimes as distinctly encapsuled as a lymphatic gland, but in other cases passing gradually into the structure of the part in which they are seated, varying in size from a miliary

granule to that of a cocoanut, or larger, and in consistence from a creamy pulp to that of a cirrhosed liver, and yielding a more or less abundant milky juice. This juice, when examined microscopically, is almost sufficiently diagnostic, for it contains none of the cell-forms already described as occurring in carcinoma or the commoner varieties of sarcoma, but only small, spherical, faintly granular corpuscles, precisely resembling leucocytes or the white corpuscles of the blood. With these there may be free granules and a few somewhat larger distinctly nucleated cells. It is, however, only when thin sections are taken from bits of the tumour hardened in chromic acid solution that the true structure is seen.

Sections thus prepared show a fine homogeneous-looking network, enclosing in its meshes, either singly or in small clusters, the pale spherical corpuscles seen in the juice. In

FIG. 18.

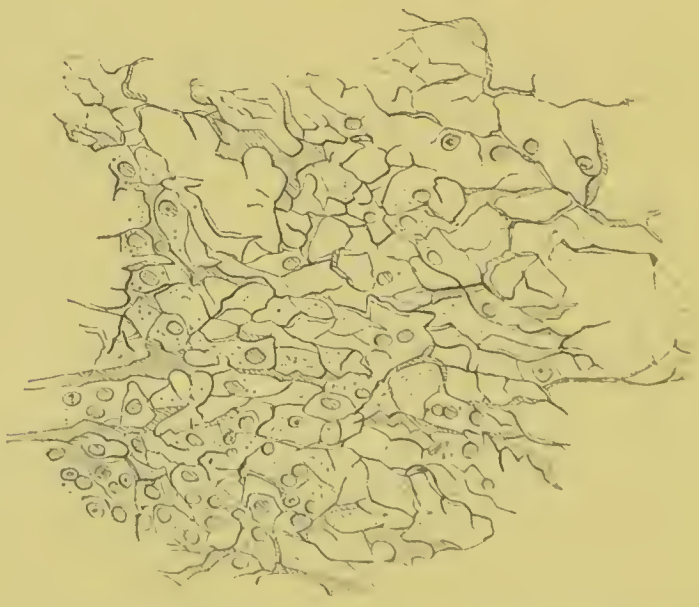

FIG. 18.—Very thin section of a lymphadenomatous tumour penciled out under water, showing the delicate irregular network and a few remaining corpuscles. Magnified 220 times.

the early stages nuclei are to be distinguished in certain of the angles of this network just as in the stroma of a lymphatic

gland; but in the later stages—those generally presented to the surgeon—the network is formed of stouter fibrils, in which the nuclei are less apparent. The structure then closely resembles that of a lymphatic gland in a condition of irritative induration; and it is this structure, with the fibrillated stroma more or less largely developed, that forms the bulk of these tumours (Plate IV).

To see this stroma distinctly it is necessary to pencil out a very thin section under water. When the corpuscles which obscure the view have been thus mostly chased away, the irregular network is clearly visible. In the foregoing sketch (fig. 18) this has been done, and the thickened network shown is a fair sample of the usual structure of these tumours, although the absence of nuclei from the angles of the meshes takes away the most characteristic element and that which specially distinguishes this growth from the small round-cell sarcoma. The latter, however, is so seldom accompanied by any notable fibrillation of its stroma, that a distinct small-meshed network is of itself sufficient to stamp the lymphadenomatous character of the growth presenting it. Whether these lymphoid formations originate in the proliferation of ordinary connective tissue, or whether they consist of hyperplasia of pre-existing adenoid tissue, is a question difficult to decide. In all their clinical features of rapid infiltrating growth, and implication of adjacent glands, as well as the formation of similar swellings in remote parts, they are probably as malignant as the most virulent carcinoma, and need the same treatment. The tumours differ from the similar masses present in leukæmia only in the absence of any obvious alteration in the blood. The histological structure is the same in both cases, but there is no notable excess of white corpuscles in the blood of a patient with lymphadenoma, as there is in so marked a degree in leukæmia.

Psammoma.—The tumour to which Virchow has given this name, from the circumstance of its containing "brain sand" (ψαμμος, sand), is sometimes classed with the sarcomata, although not much resembling any other member of this

group; and it is inserted here more on account of its rarity and want of recognition by English writers, than because it presents many features likely to be taken for those of cancer. The growth is found usually springing from the membranous envelopes of the brain and spinal cord, or in the choroid plexus, and it derives its peculiar aspect from the fact of its holding amidst its other elements a varying proportion of the curious *corpora amylacea*, which, when infiltrated with salts, form the so-called "brain sand" so frequently met with in the choroid plexus and in the lining of the cerebral ventricles. MM. Cornil and Ranvier have styled this tumour "*sarcôme angiolithique*," from the close connexion found by them to exist between the sandy particles and the small blood-vessels; but little as this growth is known at all, it is perhaps more familiar by Virchow's original appellation than by the more recent French name.

Psammoma may occur as mainly a cystic formation, affecting the choroid plexus, and causing cerebral symptoms only when attaining a large size, or it may assume rather the appearance of a papillary or warty growth, springing from the arachnoid or dura mater, and under these circumstances the flattened, slowly growing projection may give rise to no symptoms during life, and will attract notice only as a curiosity in the eyes of the morbid anatomist. In a specimen of the latter variety kindly given to me some weeks since by my friend Mr. Marcus Beck, the tumour was about the size of a florin, and three times its thickness, and its wart-like papillæ sprang from the inner surface of the outer layers of the dura mater, lifting up its inner layer and projecting through this, thrusting aside the ulcerated thin membrane all round. The ragged-looking papillæ were barely held together by some scanty connective tissue, and evidently contained no small amount of gritty particles, although there were no large grains such as are often met with in the choroid plexus. Examined microscopically, scrapings and teased portions (for the loose construction of the mass rendered thin sections unobtainable) showed that the bulk of the new growth was made up of

aggregated flattened fibre-like cells, having much the appearance of connective tissue elements when seen in groups. Isolated cells, however, bore a closer resemblance to delicate irregular pavement epithelium. Many vessels ramified through the growth, and the peculiar concentric bodies—the *corpora amylacea*—occupied a conspicuous place in every preparation. These bodies had generally so hard and black an outline as to resemble air-bubbles until more careful focussing brought into view a few irregular highly refracting particles in the centre, and faint concentric rings surrounding these, a bold black outline marking the circumference of the tiny spheres. Outside this strongly marked border was generally a lighter fibrous zone (fig. 19). Some of the bodies

FIG. 19.

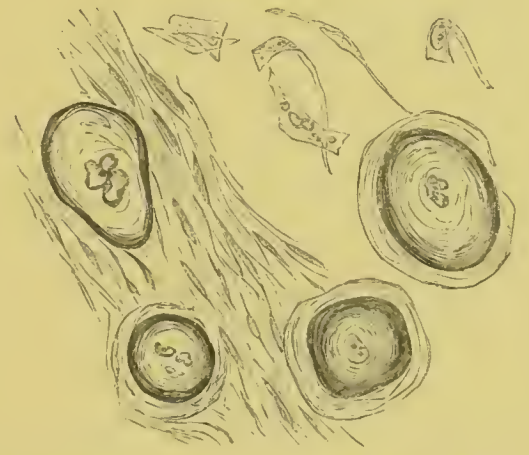

FIG. 19.—From a teased-out bit of a psammoma of the dura mater, showing the concentrically marked bodies and some detached epithelial cells. Magnified 220 times.

were pale and free from calcareous incrustation, but the majority were more or less thoroughly infiltrated. Prolonged and careful examination, however, failed to discover any connexion with the vessels such as has been described as an essential characteristic by MM. Cornil and Ranvier. The concentric structure of the bodies seemed to be brought about by the regular superposition of the delicate flattened

cells constituting the bulk of the tumour, and they bore a close resemblance to the "*globes épidermiques*" of epithelioma, the tendency to infiltration with calcareous salts forming their chief distinction from these.

Whether these tumours should be classed with the epithelliomata or simple papillomata, and what may be their origin and history, are questions interesting to the pathologist rather than to the practical surgeon, who is so little likely to encounter them that some apology is necessary for introducing them at all into a work whose scope is avowedly purely practical.

CHAPTER IX.

Epithelioma—Its Distinction from Carcinoma—Its Minute Structure—Columnar-cell Epithelioma—Rodent Cancer.

These sketches of the various new growths commonly called cancers, would not be complete without a reference to the well-known disease which, from its cancer-like nature, has been usually styled "cancroid"—a term which is objectionable from its vagueness, but which aptly enough expresses the clinical characteristics of the disease.

For Epithelioma—by which is meant a new growth furnished by the proliferation of the epidermis, or by the epithelium of the mucous membranes—although sometimes in its later stages thoroughly malignant, affecting chain after chain of lymphatic glands, and cropping up luxuriantly in remote viscera, as the heart and lungs, is yet a growth far more under surgical control than any of those which we have been considering. For while with our present mode of operating we hesitate to affirm too boldly that we can eradicate a scirrhous cancer by cutting it out, there are few surgeons who would deny that they have finally extirpated a small epithelioma of the lip or scrotum by a comparatively trifling operation.

So it is that this disease has been almost always separated somewhat from the true cancers, whilst some able observers—the late Mr. Collis, of Dublin, for instance—have refused to place it in the same category at all. And yet the more modern pathologists, as Billroth and Rindfleisch, merely regard it as a variety of carcinoma, affirming a close analogy of minute structure in the two growths, and pointing to the

difference of origin of their cells—glandular, or surface epithelia—as constituting the sole claim to separation into distinct varieties.

Nevertheless, although both growths are made up of epithelial cells and stroma, and in certain points are closely analogous, I cannot help thinking that we, in England, are wise in keeping them distinctly apart; for both in coarse physical appearances and in minute structure the disease to be now sketched differs from that which we have studied under the head of carcinoma as widely as it differs from it in the far more important features of clinical history and symptoms.

An epithelioma of the cutaneous surface, occurring usually as a shallow hard ulcer with thick fungous edges, presents a favorable specimen for exhibiting the characteristic microscopic structure of the growth, as well as its mode of origin and of invasion of the neighbouring parts. On examining a thin section from the margin of such an ulcer, one is at once struck by the fact that although here, as in carcinoma, we have before us clumps of epithelial cells in an irregularly alveolated stroma, yet the cells now differ hardly at all—save, perhaps, in their size and active nuclear proliferation—from the normal epidermis cells from which they have descended. We lack here the rich variety of cell-forms which supplant the small regular gland epithelium in carcinoma of the mamma, for instance, and at the same time we notice how comparatively slight are the fatty changes occurring in the misplaced epidermis scales. They dry up, shrivel, become squeezed by circumferential pressure into curious onion-like masses—the "*globes épidermiques*," "epithelial pearls," or "bird's-nest bodies" met with wherever excessive epidermis growth is in progress, but in singular and characteristic abundance in epithelioma (see fig. 20, *a*, and fig. 21, *a*)—or they become distended with colloid material (fig. 20, *c*); but they seldom undergo much oily degeneration, save where inflammatory or ulcerative changes are actively at work. The cells further show a great tendency to cohere by their

margins, as do normal epidermal cells, and sometimes present beautiful objects for examination with the higher powers, by

Fig. 20.

Fig. 20.—Elements from an epithelioma of the lip. Magnified 220 times. *a*, An epithelial pearl, showing the production of these bodies by the multiplication and subsequent flattening of squamous cells; *b*, serrated cells; *c*, cells containing colloid matter.

dovetailing together by finely serrated edges, after the fashion of the upper cells of the healthy rete mucosum (see fig. 20, *b*). In fact, the new growth seems to consist simply of masses of surface epithelium, which, instead of appearing above and between the papillæ, dip down amongst the connective tissue, and there actively multiplying and thriving as much from the unwonted supply of fluid nourishment as from the absence of the desiccating process to which they are normally subjected as they are pushed on towards the surface of the body, form large tubular and branching collections, capable of more prolific development the further they are removed from the surface, and at the same time more freely subjected to the risk of single cells being taken up and hurried away in the lymph- or blood-streams to form similar collections elsewhere.

This seems to be, indeed, what really happens in the formation of a primary epithelioma. Why this invasion of

the subcutaneous tissues by epithelial elements takes place in certain cases, when all the physical conditions favorable to its production must be frequently present in any wart or condyloma, it is not easy to say; but there is nothing in the process, so far as we can observe it, to justify us in assuming a special condition of the blood as its determining cause, whilst the dispersion of the disease throughout the body—rarely considerable in its extent, seldom involving more than the nearest chain of lymphatic glands, and always presenting the same epidermis-like scales wherever the secondary growth springs up—is thoroughly and solely suggestive of transference of cells of the primary tumour and their multiplication in their new seats.

Thus, the one essential anatomical feature of epithelioma is *the presence of proliferating epidermal cells in abnormal situations.* So long as the change is limited to an excessive development of surface epithelium, with, it may be, considerable enlargement of the papillæ, the growth is a papilloma; or if the proliferation commence in a sebaceous gland, so long as the result is a mere accumulation of gland epithelium within the gland walls, this may go on to almost any extent, and be accompanied by secondary fatty changes, but the only issue will be a more or less inconvenient "atheromatous cyst"—both purely innocent formations. But once let the boundary be broken through, and the cells penetrate the deeper tissues, and lymphatic (or even vascular) infection may take place at any time—in all probability with a rapidity in proportion to the movement and moisture of the affected part;[1] and with such infection the growth

[1] In the paper contributed to the 'St. Thomas's Hospital Reports' for 1871, to which reference has been already made (*vide* footnote, p. 10), I have tabulated seventy-three cases of epithelioma recorded by me in the cancer tables of the Middlesex Hospital, with the object of setting forth this connection which exists between the physical conditions of locality and the malignancy of the disease. It is there shown "that the cases showing contamination of the glands and other parts are precisely those in which the growth is subjected to the greatest amount of movement. Thus, in the lip, tongue, genitals, groin, hand, and heel, the glands were affected in from 50 to 100 per cent. of the whole

passes at once from amongst the innocent tumours to the cancers.

Whilst the *cells* of an epithelioma, therefore, differ in a marked degree from those of a carcinoma, and by reason of their tendency to mutual cohesion are not nearly so liable to be carried off to distant regions, the *stroma* is equally to be

Fig. 21.

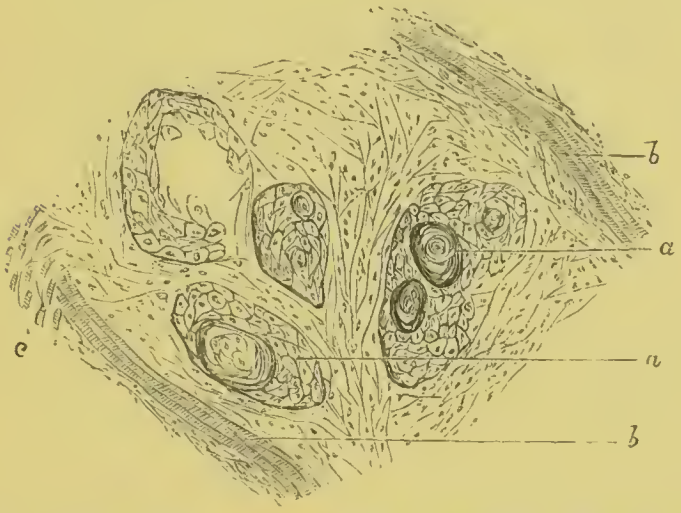

Fig. 21.—Section through an epithelioma of the tongue. Magnified about 40 times. *a*, Clusters of squamous epithelium containing some "pearls," and surrounded by a fibro-corpuscular growth, furnished by the normal connective tissue of the part; *b*, striped muscular fibres; *c*, striped muscle divided transversely.

distinguished from that of carcinoma. In fig. 21, which represents an epitheliomatous infiltration of the muscular portion of the tongue, the large squamous cells which have penetrated from the dorsum are seen to lie in detached clusters in the midst of a fibro-corpuscular stroma, striped muscle-fibres appearing on either side. This stroma is here clearly derived from the inter-fibrillar connective tissue of the tongue, the invading epithelial growth being preceded

number of cases; whilst the disease attacking the less movable parts of the face spread to the glands in a proportion of only 21·7 cases, and in the leg and scrotum remained absolutely local."

by a small-celled infiltration, suggesting irritative hyperplasia of the connective-tissue nuclei—just such a structure as is to be met with in the neighbourhood of any active growth, and only to that limited extent deserving the name of a new formation.[1] Hence we have here nothing like so regular an alveolar fibroid stroma as supports the cells of a carcinoma, although the increased connective-tissue growth, with probably an undue vascular supply, occupies in epithelioma an analogous position to that structure.

The coarse characters of epithelioma, the thick, mushroom-like elevations, the indurated excavations, the slow but destructive march, and the scanty, perhaps fetid, discharge, as well as the common site—an old wart, scar, or edge of an ulcer, or, in healthy parts, specially the line of junction of skin and mucous membrane, as the lip or vulva—suffice to render the diagnosis of the disease generally easy, and they are too familiar to need description here. The cut surfaces of these growths yield but a scanty juice, and what does exude is thicker and more curdy or ground-rice-like than the thin, milky juice of carcinoma, and under the microscope the cell-forms are usually tolerably characteristic (fig. 22).

Where similar changes affect such mucous surfaces as are clothed with columnar epithelium, the resulting new growth presents a corresponding variety of appearances, the cells being mostly arranged in the same way, and bearing a like relation to the stroma of overgrown connective tissue. But from the peculiar cell-forms present in these cases, and the greater moisture and vascularity of the parts affected, both

[1] It is interesting to note that, just as Cornil and Ranvier have described direct communication between the lymphatics and the stromal alveoli of carcinoma, so Köster states that the tubes of squamous epithelium which dip down from the surface into the deeper parts lie within lymphatic vessels. This is, however, an opinion which has not been generally accepted, and although it would certainly explain very simply those cases in which gland implication occurs, such extension of the disease is not nearly so constant nor so early as one would expect it to be, did the first traces of the morbid infiltration bear such close relation to the lymphatic channels as Köster indicates.

the superficial and the microscopic characters undergo considerable and striking modifications.

Fig. 22.

Fig. 22.—Scraping from a coarse epithelioma of the arm. Magnified 220 times.

Such growths occur not infrequently in the stomach and intestines. Where they clearly originate in a proliferation of the lining cells of the tubular glands they are often called "adenomata;" but since secondary growths having the same structure are met with occasionally in the liver and elsewhere, and since the only difference between these tumours and those surface epitheliomata which take their rise in the sebaceous glands of the skin is based upon the distinct forms of the cells furnishing the starting-point of each, it seems inconvenient to make such "adenomata" a special variety of new growth, and, with some pathologists, to speak of them as "adenoid carcinomata."

In the specimen figured in Plate V, figs. 1 and 2, both the superficial and the glandular forms of the disease were present. The patient died with peritonitis resulting from the rupture of a soft gelatinous tumour of the ileum, which had been thrust by an intussusception of the bowel through the ileo-cæcal valve. After death it was found that an

alveolated delicate stroma, containing chiefly roundish cells, occupied the submucous tissue all round the gut, whilst the villous mucous membrane covering the growth was thickened by great enlargement of the villi and proliferation of their investing columnar epithelium. Here the disease seemed to have originated in an overgrowth of the gland tissues of the bowel forming the alveolated structure with its contained exaggerated cell-elements, whilst the increased surface epithelial growth occurred probably as a consequence of this development.

Rodent Cancer, as the well-known "rodent ulcer" was styled by the late Mr. C. H. Moore in his treatise on the subject, although, no doubt, sometimes presenting clinical features which sufficiently warrant its being grouped amongst the cancers, yet does not seem to me to possess any properties, either clinical or anatomical, which justify its being placed in a distinct class by itself. The portion of Mr. Moore's book which deals with the histology of the subject is not characterised by the admirable clearness of the rest of the essay; but the want has been amply supplied by a paper in the last volume of the 'Pathological Transactions' by Mr. Hulke. Mr. Hulke gives a lucid description of six cases of rodent ulcer, and subjoins beautiful drawings of the microscopical appearances present. In all of these instances the growth was the same—an infiltration of the irritated subcutaneous connective tissue with a small oval-cell growth, whose elements were exactly comparable to the cells of the rete mucosum of the skin, these cells being arranged in large masses or in smaller bud-like processes. It would hence appear that in these cases the new growth consisted of a proliferation and deep infiltration of the undermost cells of the epithelium. In examinations made by myself of instances of well-marked rodent ulcer, I have found, besides the cell-growth described by Mr. Hulke, more distinct evidences in some of the thicker parts of the edges of the ulcers of ordinary squamous-cell epithelioma, with even rough "bird's-nest" bodies (such as are described as occasionally present

in Mr. Moore's work); and I am therefore inclined to group these "rodent ulcers" with the epitheliomata, explaining their very slow progress and comparative immunity from gland contamination by their situation—always to a great extent free from movement, moisture, or rich vascular supply.

CHAPTER X.

PRACTICAL SUMMARY.—The Prognostic and Therapeutical Value of the Accurate Diagnosis of the Varieties of Cancer—The Relative Value in this Differential Diagnosis, of Family History, Age of Patient, Cachexia, Lymphatic Gland Involvement, Adhesion by Infiltration, Pain, and Rapidity of Growth of the Tumour—Table showing these Points.

IN the preceding pages an attempt has been made to furnish practical illustrations of the essential features of the anatomy of the several forms of new growth commonly called cancers. Abstract questions of pathology have been avoided in the endeavour to furnish such a *résumé* of the subject as may be of real service to the practical surgeon. But the old cry against the microscope, "*Cui bono?*" may occur to those who read these accounts of minute structure, unless some attempt be made to deduce from all these observations some useful rules for guidance in diagnosis, prognosis, and treatment.

It has been lately said by one whose opinion justly carries with it great weight:[1]—"However instructive it may be to trace the analogies of morbid growths amongst themselves, or to establish differences between them and the natural structures, the value of the whole knowledge gained, if it ended there, would be outweighed by a single case of life prolonged or suffering averted through sounder views of treatment based upon it." Now, there is no doubt that the common impression is that these investigations into the minute structure and habits of tumours are more interesting than useful, and that they are not calculated to throw much light upon the question of treatment.

[1] Mr. Campbell De Morgan, Preface to 'The Origin of Cancer,' p. v, 1872.

But I venture to think that those who hold such opinions do not regard the matter in a sufficiently broad aspect. The struggle now being made to obtain a due recognition of the various distinct growths hitherto included under the head of cancer, is only a repetition of many such efforts which have been made in other branches of medicine of late years.

It is not so very long since diseases very different were grouped together under the title "Continued Fever." The laborious observations of such workers as Jenner, Stewart, and Murchison, have shown in what very important details the several fevers differ; and already our advance in diagnosis has not only affected materially the confidence of our prognosis in these cases, but, although we are still unable to *cure* a fever, we derive therefrom most valuable aid in conducting its treatment; and, most important of all, we have already made great strides in prophylaxis, and may expect to do a great deal more in this direction, as exact knowledge of the subject becomes more widely diffused.

In like manner it is probable that, if we steadily work on at the minute structure of tumours, and take care to associate with the points so made out the symptoms to be noted at the bedside, and during their whole course, we shall be before long in a position to say, not only that a given tumour having a special structure is probably malignant, but we shall be prepared to encounter special glandular conditions, we shall be able to predict where, when, and under what circumstances the tumour may be recurrent, and we shall be able to apply the appropriate treatment.

For it is extremely unlikely that all these tumours are to be met with the same remedy. Granted that so-called "constitutional remedies" have always failed to cure new growths, it is yet a matter of history that hosts of tumours *have* been permanently arrested in their progress, and it is also a matter of history that amongst these have been included not a few instances of genuine cancer.

But it will be only when we are thoroughly well versed in the art of the accurate differential diagnosis of tumours, that

we can hope to test fairly and profitably the many remedies which have been proposed from time to time as substitutes for excision. Such remedies have always hitherto been speedily laid aside when it has been found that many cases of cancer have pursued their fatal course unchecked by them. But if we could discover, by a careful consideration of the anatomical structure of these growths, which of them are likely to yield to other means of controlling cell-development than cutting out the part, we might decide with far greater confidence than has hitherto been possible upon the value or worthlessness of any proposed plan of treatment.

The main characters upon which reliance has hitherto been placed for the recognition of malignant disease are, the family history, the age of the patient, the cachexia, the lymphatic-gland enlargement, the adhesion to surrounding parts by infiltration of tumour elements amongst the natural tissues, the pain, and the rapidity of growth of the tumour.

That all these points have a more or less important bearing upon the diagnosis of a malignant growth is now generally admitted. Their relative importance as distinctive features of the several varieties of cancer is a far more difficult question, and one upon which we are still hardly prepared to speak with any confidence. The following suggestions, therefore, are offered with much diffidence, as the path opened by them has as yet been but little explored, and a far wider experience of cases examined and recorded with the utmost accuracy will be needed before trustworthy rules can be laid down for the guidance of surgeons.

The *family history* must necessarily be almost useless in this more particular inquiry. The most that we can learn on this head is, whether to the patient's knowledge any members of the family have suffered from tumours or swellings of any kind. Of course we can never rely upon any attempt to fix the precise nature of the tumour so inherited. But if we could gain such accurate information it would probably be of some service, for there are not wanting in the annals of surgery remarkable instances of the hereditary

descent of such easily recognisable growths as warts and fatty tumours, in which the type of tumour was handed down with great distinctness. On the other hand, it must be remembered that in the matter of hereditary descent the different tumours are apt to interchange in a puzzling degree, the offspring of a mother dying of scirrhus of the breast developing epithelioma of the lip, and *vice versâ*. Such examples of change of type of malignant tumours are so frequent as to prevent us from expecting any great assistance from accurate knowledge of family history.

The *age of the patient* is a fact of greater value. Thus, of tumours of the eyeball, almost all occurring in infancy or early childhood are gliomata; in youth and manhood sarcoma (usually springing from the choroid) is more common, and as a rare affection of advanced age carcinoma may be encountered. Affecting other parts, it has long been known that scirrhous carcinoma is most frequent between the ages of forty and fifty, rarely seen before twenty, and not very common after sixty. (It may be further noted in this connection, that the most chronic, indolent, and so most favorable cases of scirrhus, either for operation or for letting alone, are oftentimes those appearing at an advanced age.) On the other hand, sarcoma is a disease of much earlier life. The youngest children suffer with sarcoma, whilst it is especially frequent in early adolescence. So many different forms of growth are included, without distinction, under the head of "medullary cancer," that the data hitherto collected, with the view of showing the average ages at which soft cancer appears, are of no value for our present purpose. Epithelioma has been carefully observed, with the result of placing it amongst the growths occurring latest in life. Certainly the epithelioma attacking the lip, tongue, or face, is a disease of very advanced life, the largest average occurring between the ages of fifty-five and sixty-five, and few cases being seen under forty. But epithelioma of the genital organs and of the gastro-intestinal tract occurs much earlier in life, although probably with nothing like the

frequency of sarcoma. Lymphoma, on the other hand, is said to be more specially a disease of youth. Not wholly so, however, for whilst one of the best examples which I have seen was in a little boy under eight, I have twice seen this growth attain terrible dimensions in middle-aged men, and at the present moment I have under my care a woman over fifty in whom the disease has but recently appeared.

The *cachexia* is an element of no value from any point of view. Since the various symptoms usually grouped together to form this sign depend wholly upon the ravages made upon the general health and strength of the patient by the presence of a noxious local ailment, and not—so far as can be observed—upon any pre-existing taint of the system, the amount of cachexia present will vary with the amount of hæmorrhagic or fetid discharge, pain, sleeplessness, mental disquietude and interference with ordinary habits of life, and it will therefore be present in each variety of cancer according to the extent of local disturbance caused by the tumour.

Lymphatic-gland involvement is a sign of the greatest service. It is true that the lymph-glands are very prone to simple enlargement, from the presence in their neighbourhood of any source of irritation. But this inflammatory engorgement, although it may lead to glandular hyperplasia and subsequent induration rather than to suppuration, may usually be distinguished with facility. For here the patient himself commonly first perceives the swelling and draws the surgeon's attention to it. The lump is almost always tender, and, if near the surface, the skin covering it is slightly red and tense. On the other hand, the enlargement from new growth is a slow, painless, firm, perhaps nodular, swelling, scarcely at all tender, and attaining considerable size before the patient is conscious of its presence. The most puzzling cases, and those in which error is most frequently committed, are instances in which the active new growth in the gland sets up ordinary inflammation, which may rapidly run on to suppuration, and so mask the more important morbid change. This complication is particularly frequent in lymphatic

glands the seat of epithelioma, and in such cases one may learn a good deal by an examination of the grumous, flaky pus discharged, and the irregular excavated ulcer left when the pus is evacuated. *Lymphoma* usually commences in the lymphatic glands, and only takes on its infiltrating characters at a comparatively late stage. In this disease it is common to meet with several chains of enlarged glands. In *epithelioma* the glands are specially liable to suffer, and probably—as I have elsewhere endeavoured to show—in direct proportion to the mobility, moisture, and vascularity of the seat of the primary growth. In *sarcoma* the lymphatic glands nearly always escape infection. Where they are involved the growth is usually of the round- or oval-celled kind. In *carcinoma*, on the contrary, the lymphatic glands are so constantly affected, that their condition in a doubtful case of scirrhus furnishes a sign of the first diagnostic importance. I have two or three times seen breasts removed by surgeons of great experience for scirrhous carcinoma, in which nearly every other sign but this was present, but in which the subsequent examination of the specimen showed the growth to belong to the class of adenomas or chronic mammary tumours rather than to the true carcinomata.

The importance of this observation has been recently brought forcibly home to myself by a mistake made by my not paying sufficient attention to it. The patient, whom I saw in consultation with my friend Dr. Rice, was about forty years old; she had lost a sister with cancer, and for five years past she had noticed a hard lump in the left breast. She saw several surgeons about it soon after its first appearance, but no definite opinion was pronounced upon it. During the last year, after some mental distress, the swelling rapidly increased, and became the seat of occasional severe dragging pains. The nipple now began to be drawn in, one or two other smaller, very hard points became apparent in the breast, and the general health began to fail. She consulted two or three surgeons, and was strongly advised to

submit to an operation without delay. I removed the whole breast in this case with the greatest care, convinced that it was scirrhus, although there were no enlarged glands in the axilla. Happily the wound healed almost entirely by first intention, and the result of the microscopic examination prevented me from regretting the operation; for if only the larger tumour had been removed, subsequent measures would have been needed for the smaller growing ones. But the tumours were none of them carcinomatous. They were made up of new, rapidly growing fibrous tissue, enclosing islets of mammary gland structure, and their extreme hardness was caused by their compression within very tight capsules, which completely shut them off from the rest of the gland. In this case the error was committed of relying too much upon such signs as the hardness of the lump, retraction of the nipple (from which, however, there had never been any discharge), the severe intermittent pain, the condition of the covering skin, which could not be freely pinched up over the tumour, although not distinctly adherent to it, and the recent appearance of other smaller hard lumps in the breast. Scirrhus very rarely lasts for so long, and then takes on a rapid increase, without infecting the axillary glands. *Glioma* may affect the lymphatic glands, but it very rarely extends in this way until a late stage in the disease has been reached.

The adhesion to surrounding parts by infiltration of tumour elements amongst the natural tissues is of far less value in distinguishing the varieties of cancer than as a general indication of malignancy. In the latter regard it can hardly be ranked too highly, but the habits of many of the new formations are so capricious in this respect as to render the sign of little further service. Epithelioma, indeed, is always a genuine infiltration from the first, and the same may be said of carcinoma in the vast majority of cases. But occasionally a growth having a true carcinomatous structure, and affecting the lymphatic glands, may be distinctly encapsuled, pushing aside enveloping muscles without invading them—as I have seen a carcinoma to do, springing from the femur—

or, as happened in a case upon which Dr. Cayley reported with me to the Pathological Society of London, a scirrhous carcinoma of the breast may be imbedded in the wall of a large cyst, and show no tendency to spread beyond the limits of the cyst.

Sarcoma is also—so far as my experience goes—as often an obviously infiltrating growth as it is encapsuled. In the illustrations appended to this volume will be seen more than one example of admixture of the sarcoma elements with those of the healthy tissues of the part invaded, and the point is further referred to in the chapter on sarcoma. The like uncertainty attends lymphoma, which, is, however, usually distinctly limited in its earlier stages. Glioma is always an infiltrating growth.

Pain is a symptom from which something may be learnt, but not very much, for the pain caused by tumours seems to be almost wholly due to the local disturbance of the normal tissues, and therefore the structure of the growth has less to do with the production of pain than have the accidents of its locality or the rapidity of its increase. Although, as a rule, pain is a far more constant concomitant of malignant than of innocent growths, it is not a very reliable sign even to this extent. I recently removed a rapidly growing lipoma from the back of a young woman, whose attention had been first attracted to the lump by the occurrence of sharp shooting pains in its neighbourhood. The severe lancinating and intermittent pains of scirrhous carcinoma are probably due to the tendency to fatty decay of the central cell elements, and the subsequent contraction upon them of the fibroid, cicatrix-like tissue forming the stroma of the growth. This contraction causes a dragging upon the surrounding parts, which seldom attends the softer malignant growths, and hence the pain of these is rarely so severe or of the same dragging or piercing character. Large, full, rapidly growing sarcomata have usually only a dull, constant, throbbing pain, unless special nerves be pressed against. Lymphoma seems to be little attended with pain. When affecting the glands

of the anterior mediastinum, for instance—a frequent seat—pain is only complained of when the growth attains such a size as to interfere more or less considerably with respiration. So, too, in the lymphomatous tumours of the neck and axilla, the pain complained of is very slight, until their size causes pressure upon the nerve trunks in the vicinity, which is betrayed by the onset of occasional shooting pains down the arm or over the head and neck.

In like manner the earliest stages of epithelioma are usually quite painless, although perhaps no disease is productive of more excruciating agony than this in its later periods of deep ulceration. The sufferings of a patient with advanced epithelioma of the tongue are so distressing to witness, that in many cases an operation confessedly inadequate for the removal of the disease may be desirable as a partial relief from the patient's intense misery.

Colotomy may relieve much of the great distress occasioned by an epithelioma of the rectum, and accordingly it is rapidly finding favour as a valuable palliative measure with surgeons who see much of this disease.

In the case of a hospital patient on whom I recently performed this operation for extensive malignant disease of the rectum, there has been absolutely no return since of the pain, which before had been at times extremely severe and accompanied by inability to retain the fæces. Since the operation, healthy motions have passed regularly by the artificial anus, and the improvement in the general health has been most marked and gratifying.

Lastly, the *rapidity of the growth of the tumour*, like the former sign, throws little light upon the precise nature of the growth. As a general prognostic sign in malignant disease it is of much value, but the several growths vary so greatly in their rate of progress—this being apparently affected by any condition influencing the general health of the patient, and as often following a capricious course without any obvious determining cause—that the rapidity or slowness, or chequered course of the growth of a tumour

cannot be said to bear any constant relation to its intimate structure.

The following table shows at a glance the relative value of the several symptoms which have been now enumerated. If extending experience should confirm these views, and, by correcting present misapprehensions, teach us how to discriminate more justly and certainly between the various tumours which we are called upon to treat, we may hope before very long to add to our knowledge of morbid anatomy such sound therapeutical principles as may rescue cancer from the hands of empirics, and place it in its various forms amongst the best known if not the most successfully treated of surgical ailments.

Table showing relative Diagnostic Value of usual Signs of Malignancy in the several Forms of Cancer.

	Carcinoma.	Sarcoma.	Glioma.	Lymphoma.	Epithelioma.
Family history	Distinct hereditary disposition not unfrequent.	. . . . .	Of little use	. . . . .	Ancestors often subject to other forms of cancer.
Age of patient	Chiefly 40—60; very rare before 20.	Infancy, youth, and early adult life.	Infancy.	Common at any age, but chiefly before puberty.	Chiefly after 50; earlier in internal parts.
Cachexia	. . . . .	Depends upon extent of local ravages.			
Lymphatic gland involvement	Extremely frequent and early.	Very seldom encountered.	Occurs in late stages only.	Very extensive from the first.	Common in later stages, in proportion to mobility and vascularity of affected part.
Infiltration of surrounding parts	Always infiltrating, with very rare exceptions.	Often encapsuled.	Never encapsuled.	Encapsuled at first, but soon infiltrating.	Infiltrating from the first.
Pain	Usually severe, intermitting, and lancinating.	Seldom severe; usually dull or throbbing.	Very little, if any.	Only by pressure on neighbouring nerve trunks.	Extremely severe in later stages.
Rapidity of growth	Capricious; usually rather rapid.	Usually very rapid.	Rapid.	Uncertain; sometimes very rapid.	Usually slow; rapidity depending on local conditions of mobility, &c.
Microscopic structure	An alveolar fibroid stroma, containing epithelioid cells in clear fluid.	Almost entirely cellular, with some visible intercellular substance; cells of spindle, round, or oval type.	Small round cells in soft intercellular substance.	Fine network, holding lymphoid corpuscles in its meshes.	Infiltration of surface epithelial elements amongst deeper structures, with common tendency to formation of "nests."

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